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SKIN CANCER

Prickle-celled cancer originating in an old lupus vulgaris lesion.
(Collection of Dr. M. L. Heidingsfeld.)

SKIN CANCER

BY

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TO

WILLIAM STEWART HALSTED

A True Student of Cancer.

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PREFACE

When one considers that epithelial growths of the skin, both benign and malignant, are so common, that they are usually so easily diagnosed, that the tissue from them is readily obtainable for histological study, and that most of them are so amenable to proper treatment, it is surprising how much ignorance prevails concerning them, even among surgeons and dermatologists. In this country Bloodgood has done much to correlate the clinical and pathological findings, and to point out how these different findings influence treatment, for the treatment of tumors of the skin must be conducted by different procedures according to their malignancy.

In this book an effort has been made to gather under one cover the latest views on malignant tumors of the skin, and to give the personal experience of the author, an experience gained in Dr. Bloodgood's surgical pathological department of the Johns Hopkins Hospital, in Dr. Gilchrist's dermatological clinic at the same institution, and in the surgical, pathological, and dermatological departments of the Freedmen's and Georgetown University hospitals.

The aim of the book is to be both scientific and practical—to give the correct pathology of the cutaneous neoplasms, and to point out how this guides treatment.

It is a pleasure to thank my friends for the help that they have given me, in the referring of cases for study, in the preparation of pathological material, and in furnishing me photographs. My thanks are due to Dr. Richard L. Sutton, of Kansas City; Dr. M. L. Heidingsfeld, of Cincinnati; Dr. C. J. White, of Boston; Dr. George M. MacKee, of New York; Dr. Perkins, of Kansas City; and Dr. Gilchrist for illustrations. Both Dr. Gilchrist and Dr. E. A. Balloch, of Washington, have allowed me to make free use of their material. Dr. Wm. B. Sowers, of Washington, for several years resident surgeon at the Johns Hopkins Hospital, has written the entire subject of carcinoma of the lip, and Dr. H. A. Fowler, of Washington, has helped me with the subject of cancer of the penis. Dr. Van Sweringen, pathologist to Freedmen's Hospital, has prepared many sections for me.

H. H. HAZEN.

Washington, D. C.

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SKIN CANCER

CHAPTER I.

GENERAL CONSIDERATIONS.

DEFINITION AND CONCEPTION.

In 1863 Virchow[1] stated that it was practically impossible to give a satisfactory definition of a tumor, and many writers since that time have unwittingly proven the truth of that statement. In dealing with epithelial neoplasms we may, however, say that any autonomous growth of epithelial cells, or of cells derived from the epithelium, constitute a neoplasm. We are not dealing with inflammatory masses or with cysts, although either of these conditions can, and do, give rise to tumors, sometimes clinically indistinguishable from true neoplasms.

CLASSIFICATION.

A thoroughly satisfactory classification of epithelial tumors has not yet been made. For this there are many reasons; first and foremost, because until a few years ago the pathology was not thoroughly studied, and no one recognized that a tumor showing one type of structure might, in the natural course of events, come to present a totally different histological picture, although the same cell type was always preserved. Then, too, the use of the terms "epithelioma" and "carcinoma," not to mention the rest of the nomenclature, has varied markedly at the hand of different writers, and even today there is no uniformity. The use of the term "papilloma" is a splendid illustration of this, for the word is used to cover almost any tumor that projects at all above the surface of the skin or mucous membrane.

According to Unna,[2] the first division of carcinomata of the skin was made by Hannover[3] in 1852, when he made use of the terms "flat" and "infiltrating," a division that was brought into popu-

[1] Virchow: Die Krankhaften Geschwülste, Berlin, 1863.

[2] Unna: Histopathology of Diseases of the Skin (Walker's translation), New York, 1896.

[3] Hannover: Das Epithelioma, Leipzig, 1852.

larity in the great work of Thiersch[4] in 1865. And yet Thiersch recognized that an epithelial cancer of a flat or apparently benign nature might come to infiltrate the tissues very deeply. For a further criticism of Thiersch's views the reader is referred to pages 665 to 668 of Unna's book, although it must be clearly understood that the author by no means coincides with all of Unna's beliefs and criticisms.

To some extent Thiersch, and to an even greater extent many subsequent writers, have attempted to classify cutaneous carcinomata according to the tissue from which they sprang. There are, of course, the following possible courses for epithelial tumors:

1. The various layers of the epidermis.
2. The hair follicles.
3. The sebaceous glands.
4. The sweat glands.
5. The sweat ducts.
6. Congenitally misplaced epithelial structures or cells.

Unfortunately for this plan, none of its advocates have been thoroughly good pathologists, and hence there have been many glaring errors. For instance, any carcinoma with the cells arranged in a hollow cylinder at once had its origin ascribed to the sebaceous glands, which notion, of course, is an absolutely erroneous one. For a more detailed account of these fallacies the reader is again referred to Unna.

Unna's own classification deserves especial notice because he is a thoroughly well-trained pathologist, has studied the question carefully, and has made an effort to give a satisfactory classification. An abridgement of his classification is as follows:

I. Malignant new formations.

A. Carcinoma vulgare.

1. Fungating forms.
   a. Papillary.
   b. Coarse reticular.
2. Cylindrical forms.
   a. Reticular.
   b. Simple cylindrical.
   c. Acinous.
   d. Styloid.

[4] Thiersch: Der Epithelkrebs, Leipzig, 1865.

3. Alveolar forms.
   a. Large alveolar.
   b. Small alveolar.
4. Carcinomatous lymphatic infarctions.
   a. Carcinoma Jacob, rodent ulcer.
   b. Carcinoma of the sailor's skin.
   c. Xeroderma pigmentosum.
   d. Paget's carcinoma of the nipple.
   e. Nevo- and melano-carcinomata.

II. Benign new formations.

A. Tumors proper.
1. Of the epidermis.
   a. Acanthoma, including
      Verruca vulgaris.
      Condyloma.
      Epithelioma (molluscum) contagiosum.
      Acanthosis nigricans.
2. Glandular hypertrophy and adenoma, including
   a. Hypertrophy and adenoma of the coil gland apparatus.
      General hypertrophy.
      Spiradenoma.
      Syringoadenoma.
   b. Hypertrophy and adenoma of the sebaceous glands
      Sebaceous gland hypertrophy.
      Steadadenoma.

B. Stagnatory tumors.
1. Of the epidermis.
   a. Keratoma, including
      Callus.
      Clavus.
      Cutaneous horn.
      Angiokeratoma.
      Onychogryphosis.
   b. Cysts, including
      Traumatic epidermis cysts.
      Follicular cysts.
      Horny cysts.
      Sebaceous cysts.

2. Syringal cysts.
   a. Duct cysts.
   b. Porous cysts.

III. Malformations.

A. Progressive disturbances of nutrition.
   1. Proliferating tumors.
      a. Syringoadenoma (lymphangioma tuberosum multiplex).
      b. Acanthoma adenoides cysticum (multiple benign cystic epithelioma).
   2. Stagnatory tumors.
      a. Dermoids.
      b. Atheromata.

Certain objections can at once be raised to this scheme. First, there is a mixture of clinical and pathological forms. Second, it treats of the less important tumors according to their origin, while it totally ignores the origin of the more important tumors. Third, it is doubtful if neoplasms can rightly be divided into "tumors proper" and "stagnatory tumors," using the latter expression, in Unna's sense, to mean that there is not an undue proliferation of tissue, but rather a lessened destruction of it. Fourth, Unna uses the term "acanthoma" to apply to the basal cells as well as to the prickle cells of the rete. This is incorrect, as "acanthoma" should apply only to the horny cells; the term "reteoma" would be more exact in many instances. Fifth, nor can the writer agree that the multiple benign cystic epithelioma is a malformation, nor does he believe that it should be called "acanthoma adenoides cysticum," for the reason that it develops from basal cells. With these few exceptions, however, Unna's classification is excellent, and a model for all future attempts.

Ribbert's[5] terminology is still very popular, especially among clinicians, for it has the merit of simplicity. According to this author we have:

Papillomas which comprise fibro-epithelial tumors.

Epitheliomas which comprise tumors derived from the surface epithelium.

Carcinomas which comprise tumors derived from glandular epithelium.

[5] Ribbert: Geschwülstlehre, Born, 1904.

As Auspitz, Unna, and many others have pointed out, the term papilloma is, histologically speaking, a grave misnomer, for the real development is in the rete and the papillæ are only secondarily affected. If all tumors arising from squamous epithelium are to be spoken of as epitheliomata, we must call malignant epithelial tumors of the lip, tongue, pharynx, esophagus, and of certain portions of the genital tract, epitheliomata. To the author this seems undesirable for two reasons; first, because these tumors run the same course as the glandular carcinomata; and, secondly, because the term carcinoma means more to both physician and laity than does the word epithelioma, especially since the latter is sometimes used to designate a benign growth.

Krompecher,[6] in his excellent monograph, "Der Basalzellenkrebs," adopts the following classifications:

1. Fibroepithelioma spinocellulare simplex, or keratodes.
2. Carcinoma spinocellulare simplex, or keratodes.
3. Fibroepithelioma basocellulare.
4. Carcinoma basocellulare { Solidum. / Adenoides. / Cysticum. / Hyalinicum, etc.

Bloodgood,[7] after a characteristic thorough search of the literature, advocated the following scheme in his teaching and for his specimens:

1. Benign epithelial warts.
   a. Mixed epithelial warts.
   b. Spinocellular (horny) warts.
   c. Basocellular warts.
2. Malignant epithelial warts.
   a. Epithelioma spinocellulare malignum.
   b. Epithelioma basocellulare malignum.
3. Malignant basocellular tumors.
   a. Epithelioma basocellulare solidum malignum.
   b. Epithelioma basocellulare solidum et adenoides malignum.
   c. Epithelioma basocellulare solidum et adenoides cysticum malignum.
   d. Carcinoma basocellulare solidum stellatum.
4. Carcinoma cubocellulare.

[6] Krompecher: Der Basalzellenkrebs, Jena, 1903.
[7] Bloodgood: Progressive Medicine, December, 1904.

5. Epithelioma spinocellulare malignum.
6. Carcinoma spinocellulare malignum.
7. Adenocarcinoma of hair follicles.
8. Adenocarcinoma of sweat glands.

Here the author seriously objects to Bloodgood's differentiation of malignant tumors, having the same origin, into epitheliomata and carcinomata according to slight differences in their histological picture. Bloodgood uses the term epithelioma when the growth has retained the picture of the tissue from which it sprang, and carcinoma when the picture of the original tissue can no longer be distinguished. In some tumors certain sections will, however, resemble epithelioma, and other sections, perhaps only a short distance away, will resemble carcinoma, and hence this differentiation does not appeal to the writer as being practical. The spinocellular warts are not necessarily horny warts; here there seems to be some confusion with the keratomata. Otherwise, however, Bloodgood's pathological classification is extremely good. In addition to giving us a working differentiation, Bloodgood has also shown exactly how the pathology of a neoplasm agrees with its clinical course, and hence with its treatment. He has added a most important chapter to the study of the malignant cutaneous tumors.

In an attempt to give a simpler classification, Bloodgood has recently devised the following classification:

1. Benign precancerous lesions.
   a. Warts, which include any epithelial hypertrophy.
   b. Subepidermal nodules, often sebaceous gland infections.
   c. Ulcers, as tuberculous, syphilitic, etc.
   d. Sinuses, unhealed.
2. Early cancers.
   a. Malignant warts.
   b. Adenocarcinomata.
   c. Epithelial hypertrophy in ulcers, and sinuses.
3. Late cancers.
   a. Spino-celled cancers.
   b. Cubo-celled cancers.
   c. Baso-celled cancers.

Inasmuch as this book is primarily intended for the clinician, it has seemed to the author to be best to give a clinical, rather than a pathological, nomenclature, and he has adopted the following:

1. Benign epithelial tumors.
   a. Keratomata.
   b. Mixed-celled epithelial warts.
   c. Spinous-celled epithelial warts.
   d. Baso-celled epithelial tumors { Nevoid. / Multiple benign.
2. Malignant epithelial warts.
   a. Spino-celled.
   b. Baso-celled.
3. Baso-celled carcinomata.
   a. Flat rodent ulcer.
   b. Button-like or nodular carcinoma.
   c. Rolled-edge carcinoma.
   d. Depressed scar-like carcinoma.
   e. Morphea-like carcinoma.
   f. Fungating carcinoma.
   g. Ulcerative carcinoma.
4. Cubo-celled carcinomata.
   a. Ulcerative carcinoma.
   b. Fungating carcinoma.
5. Spino-celled carcinomata.
   a. Ulcerative carcinoma.
   b. Fungating carcinoma.
6. Tumors of hair follicles.
   a. Benign (multiple benign cystic epithelioma of Jarisch).
   b. Carcinoma.
7. Tumors of sweat glands.
   a. Adenoma.
   b. Carcinoma.
8. Tumors of sweat ducts.
   a. Adenoma.
   b. Syringocystadenoma.
9. Tumors of sebaceous glands.
   a. Adenoma sebaceum.
   b. Adenoma.
   c. Adenocarcinoma.
10. Nevocarcinomata (and multiple pigmented carcinomata).
11. Paget's disease.
12. Carcinomata by extension.
13. Metastatic carcinomata.
14. Carcinomata en cuirasse.
15. Endotheliomata capitis.

Some authors, notably Adami[8] and Hertzler,[9] object to Krompecher's differentiation of skin carcinomata into prickle and basal cellular types, pointing out that the prickle cells are simply a differentiation of the basal cells, and are not of a different origin. But to the author this classification seems justified, for the two types of tumor run absolutely different clinical courses—courses even more distinct than the histological pictures. The basocellular tumor is usually of slow, or of comparatively slow, growth, and practically never metastasizes, thus differing markedly from the spinous-celled tumors, which grow rapidly, and usually form metastases. Krompecher also recognizes a basocellular glandular tumor, a neoplasm less malignant than the type of adenocarcinoma, in which the cell type is that of the superficial epithelial lining of the ducts. Bloodgood is inclined to agree with Krompecher in this assertion.

STRUCTURE.

All neoplasms consist of two main elements—the cells and the stroma. As has already been stated, the cells are derived from the various types of epithelial cells, and, with the exception of the tumors derived from the sebaceous glands, remain remarkably true to type unless flattened out by pressure. We can easily recognize the basal-celled and the spinous-celled type, and, with slightly more difficulty, the cubocelled type. The cells from the appendages of the skin may usually be recognized, although, of course, the tumors originating from the hair follicles may very soon come to absolutely resemble the neoplasms originating from the surface epithelium. The cell type of the sebaceous glands usually changes so promptly that it is impossible to prove that a tumor had its origin in these glands. This change consists in a loss of the fat, after which the cell is difficult to recognize.

The criterion of malignancy is the breaking through of the basal membrane by the epithelial cells. This basal membrane normally forms the limit of the epithelial cells, thus separating them from the fibrous tissue of the corium. Invasion, once the membrane is ruptured, may take place in any one of several ways, all carefully studied by Unna. The cancer cells may invade practically *en masse*, they may form more or less solid alveoli, they may push forward in long alveoli, or they may branch out like the branches of a tree, or they may invade singly or in small groups. The mode of invasion depends on at least two factors—one the inherent power of

[8] Adami: Principles of Pathology, New York, 1908, i.
[9] Hertzler: Treatise on Tumors, New York, 1912.

reproduction of the cancer cells, and the other the resisting power of the invaded tissue.

Characteristic of cancer cells are the atypical mitotic figures, a peculiarity so pronounced that some authors have been inclined to believe that the atypical power of reproduction was the cause of the disease. It is now usually believed, however, that irregular mitosis is an effect and not a cause.

The degenerations of cancer cells have been carefully studied by several investigators, including Gilchrist[10] and Unna. Both call particular attention to the close resemblance of some of these degenerative bodies to parasites, and warn against the error of mistaking them for causal organisms.

Unna states that the most common degeneration is the hyaline one, the so-called cancer pearls being one variety of this type of degeneration. The pearls are simply groups of cells arranged concentrically, and having a great affinity for acid dyes, due to the degenerative changes. Unna also describes eight forms of hyaline degeneration of the circumscribed variety. They are:

1. Round balls of a size varying from 15 to 20 microns in diameter, and in the interior of which there exist the remains of a nucleus, always lying in a cavity.

2. Irregular, long twisted bodies are fairly common.

3. Small hyaline bodies, having a diameter of from 7 to 15 microns, may lie in a nuclear cavity, but close to the nucleus.

4. The bodies described in the last heading may become elongated.

5. Hyaline rods or tendrils are sometimes found.

6. There may exist capsulated structures in which there is a well-preserved nucleus, lying in a ring-formed cell that has undergone hyaline degeneration.

7. Flake or vesicle-like hyaline bodies with nuclear cavities may occur.

8. And, lastly, there may exist hyaline vesicles in which the nuclear remains are inclosed by two hyaline capsules.

There is a final group in which exist conglomerations which have arisen from the compression and coalescence of the individual elements. There is another group of hyaline degeneration, even commoner than the circumscribed changes, and that is the diffuse hyaline change. This degeneration can be distinguished only in well-

[10] Gilchrist: Johns Hopkins Hospital Reports; Studies in Dermatology, 1896.

stained specimens, and is frequently a precursor of the more circumscribed changes. Unna states "the limited, diffused hyaline degeneration of the inner perinuclear substance of the cell-body is extraordinarily common."

Next in frequency to the hyaline degeneration is the simple softening and liquefaction of the epithelium, which is often combined with the hyaline changes. A single cell may be attacked, or a large portion of the cancer may soften. This form of degeneration is not present in those forms of cancer that grow by long, slender processes.

A few cases show keratoid degenerations; that is, the formation of true horny pearls, so named because of their gross appearance under a lens of low magnifying power. This form of degeneration occurs solely in tumors derived from the prickle layer. The cells are arranged concentrically in whorls, and are apparently under considerable pressure. Naturally they have a great affinity for acid dyes, such as eosin or orcein.

Occasionally calcification occurs in cancer, developing from the deposits of lime salts in the pearls.

The stroma or fibrous tissue is either the old fibrous tissue, which has been invaded by the tumor cells, or is newly formed. In some types of neoplasm one prevails, while in other types of tumor the other prevails. Of course there is frequently a combination of the two. Quite frequently the cancerous invasion of the corium induces a severe inflammatory reaction, some authors going so far as to claim that a cancerous downgrowth of tissue never occurs without a cellular exudate forming around it. The cells usually found are small round cells, fixed tissue cells, mast cells and plasma cells. Giant cells are occasionally found. Sometimes this reaction is so marked as to almost completely obscure the cancerous process. Unna states that in twenty-four out of his seventy cases an inflammatory reaction was very considerable; the rodent ulcers, Paget's cancers, and the cancers of xeroderma pigmentosum in particular showing much infiltration. It is very rare to find every nodule or process of invading cancer walled in by an inflammatory membrane, but some of them usually are. Unna states that in ten of his cases there was no inflammatory reaction. The cellular infiltration of the cutis is usually directly in ratio with the rapidity of infiltration by the neoplasm.

Neoplasms have a complete vascular circulation, the blood vessels may pre-exist, or may be newly formed, but are usually derived from both sources. The newly-formed blood vessels consist of an en-

dothelial lining, with occasionally a fibrous outer layer, and vary greatly in size.

According to Hertzler neither nerves nor lymphatics have been satisfactorily demonstrated.

GROWTH OF TUMORS.

Many authors think that a carcinoma springs from one center, but Petersen's[11] work would seem to show that the multicentric origin of malignant epithelial tumors is far from uncommon. As Bloodgood well observes, Petersen's demonstrations apply to the basal-celled type, a form of tumor that is frequently multiple. Petersen's work appears to have been very carefully done after the "Plattenmodellen-Methode" of Born.[12] The early tumors were cut into serial sections, and from these sections a wax model was built up. This is, of course, the only positive way in which the question as to the unicentric or multicentric origin of cancer can be settled. As bearing on this point, Gilchrist has recently had a very early basal-celled carcinoma of the face, in which, at a distance of about 3 mm. from the main tumor mass, there was a distinct new and exceedingly early carcinoma developing. Serial sections showed that there was no connection between the two. If these tumors are really of multicentric origin, the point has a great practical bearing, for it means that a wider incision is necessary at the time of operation. This fact, or rather theory, may explain why basal-celled carcinomata so often recur after operations in which but a small margin is given them. On the other hand, it must always be remembered that metastases may have taken place by a lymph channel, and that an apparently separate growth is in reality simply a metastasis.

At first it was thought that cancer spread by apposition, that the cancer cell caused the neighboring cells to also become cancerous, and later observation has shown that to some extent this belief is correct. Hertzler says: "In transplanted epithelial tumors in animals the connective tissue has been stimulated to sarcoma formation, showing that the power of growth may be transmitted to other kinds of tissue. Still more conclusive are the experiments of Borrel and Lewin, in which epidermis was stimulated to the formation of squamous epithelioma by the transplantation of glandular tumor beneath it, showing that the proliferating stimulus may be conveyed by cells possessed of the power of unlimited growth. In both these instances there can be no confusion between the normal and the

[11] Petersen: Beitr. z. klin. Chir., 1902, xxxii, 543.

[12] Born: Böhm-Oppel Taschenb. d. Mikr. Technik., 74.

tumor cells. The proliferation excited by Scharlach R. and Sudan III. likewise show clearly that epithelial cells can be made to proliferate and invade surrounding tissue by the action of certain extrinsic stimuli. It may be regarded as proven, therefore, that normal epithelial cells, under certain conditions, may be made to proliferate by close contact with malignant cells or by other stimulation.'' And yet it is generally conceded that tumor growth comes from the multiplication of the tumor cells, rather than from the conversion of other cells to a malignant type.

Growth takes place by the cancer cells either invading between the connective tissue fibers through the lymphatics or otherwise, or by bodily pushing the connective tissue aside, or more usually by a combination of both methods. These invading cells may or may not retain connection with the main body of the tumor. In the more malignant types of tumors, cells may escape to the lymphatic glands, or may be carried by blood vessels to remote portions of the body, or they may spread out and form separate masses in the proximity of the parent neoplasm. In cancer the growth usually takes place through the lymph spaces and lymph vessels. On account of this spread through the lymphatic system, it is often impossible to differentiate between metastasis and local infiltrative growth; in fact, it is desirable not to attempt to distinguish between them, for they are essentially the same. The superficial spread may be so great as to form cancer *en cuirasse,* where practically the whole subcutaneous tissue becomes cancerous. The lymph glands affected are usually the nearest glands draining the cancerous area, but rarely these are skipped and more remote ones are involved. Extension by contact is rarely seen in tumors of the skin, and many excellent clinicians deny its existence. It is very important to note that cancer cells may lie dormant for many years, and then suddenly take on great activity. We no longer speak of cancer patients as cured when an interval of three years has elapsed without recurrence.

Occasionally adenomata of the suprarenal or thyroid glands form metastases, and the author has observed one case where a histologically benign adenoma of the sweat glands metastasized to the neighboring glands. It seems reasonable, however, to suppose that there are true area of malignancy in these neoplasms.

Recurrence after operation depends on the factors already discussed. Recurrence means that all tumor cells were not removed by the surgeon, either because they had escaped to other organs, or because of a wide local spread.

TOXINS.

It has not been proven that epithelial tumors have a specific toxin. What absorption there is probably comes from the endotoxins of bacteria which are secondary invaders.

IMMUNITY.

There is probably no authentic instance where an epithelial neoplasm, microscopically proven to be malignant, has spontaneously healed, *and failed to recur.* The central portion of a rodent ulcer may heal and form scar tissue, and may likewise scab over and apparently heal for a year or even more, but not permanently; in fact, we know nothing of true immunity.

ETIOLOGY.

The causative factor in cancer of the skin is that of cancer in any other portion of the body, and is still unsolved. Dermatologists have not done their share toward the elucidation of the carcinoma riddle, although they have had better opportunities than any other type of clinician, inasmuch as they are sometimes able to trace the development of cutaneous cancer from the various precancerous dermatoses, of which xeroderma pigmentosum forms such a beautiful example. Ewing[13] has recently treated exhaustively of the different theories as to the etiology of cancer, and Loeb[14] has published a number of excellent papers.

Cohnheim's Theory.—Cohnheim[15] believed that cancer arose from congenitally displaced epithelium, beginning to grow riotously. As Unna has well pointed out, this certainly takes place in the neoplasms arising from congenital moles and from other nevi. At least three objections may, however, be placed against this theory—first, that cancer often starts where no congenital rests can be demonstrated, and where it is extremely improbable that any such rests would exist; second, that the theory does not explain why the rests become malignant; and, third, as pointed out by Welch, that even in very deep burns, where *all* of the surface epithelium is destroyed, a carcinoma may later develop. It may be added that the known congenital malformations do not very frequently become malignant.

Changes in Cell Type or Metaplasia.—While an epithelial cell of one type may be changed into an epithelial cell of another type,

[13] Ewing: Arch. Int. Med., 1908, i, 175.
[14] Loeb and Sweek: Jour. Med. Research, 1913, xxiii, 2, July.
[15] Cohnheim: Vorlesungen über allg. Pathologie, Berlin, 1877, i.

there is no proof that one type of cell may turn into a radically different type. It seems certain that metaplasia in epithelial tumors is confined within narrow limits. Of course, it is known that a benign papilloma, so-called, that has existed for years may later become malignant. But, again, this theory is not satisfying, for it gives no explanation why these changes take place.

Regression.—By this term Ribbert indicated a condition of cell change where cells become atavistic, or less differentiated. It is generally stated by pathologists that tumors arising from the less differentiated cells and showing the structure of the primitive cells are the most malignant, and yet in carcinoma of the skin we find that the basal-celled (or primary) tumors are much less malignant than the tumors arising from the prickle cells and to some extent retaining their structure. It is true that in the latter the prickles are short, or entirely lost, and that the cells are smaller than normal, but these changes may largely be due to pressure.

Atypical mitotic figures have been studied by many, and by some believed to be responsible for the abnormal proliferation of the cells, but the majority of pathologists believe that these abnormalities are the result and not the cause of bewildered growths.

Changes in Tissue Balance.—Thiersch held that in carcinomata the primary change was in the connective tissue, that there was a weakening of it which allowed the epithelial cells to expand and penetrate into it. He thought that there was an antagonism between the epithelial cells and the connective tissue cells, a totally unjustified assumption. It is well known that in many conditions, as in x-ray cancer, the primary change is in the connective tissue, but there are no facts to justify the belief of Thiersch. Hertzler has shown that in very early cases of cancer the connective tissue does not take acid stains in a normal way, but nothing practical has developed out of this interesting demonstration.

Microorganisms.—Ewing gives the following list of parasites that have at some time been held to be responsible for cancer:

Bacteria.—Bacillus of Rappin, 1886; Scheurlen, 1887; Francke, 1888; Lampiasi, 1888; Koubassof, 1889; Micrococcus neoformans, Doyen, 1902.

Coccidia.—Cocidium of Darier, 1889; Albarran, 1889; Thoma, 1889; Sjobring, 1890; Coccidium sarcolytum, Adamkiewicz, 1892; Soudakiewitsch-Metchnikoff, 1892; Monsarrat, 1905.

Sporozoa (unclassified).—Birdseye inclusion, Foa, 1891; Plimmer's bodies, 1892; Sporozoön, Ruffer, 1892; Sawtschenko, 1893; Ameba-sporidium, Pfeiffer, 1893; Rhopalocephalus canceromatosus,

Korotneff, 1893; Sporozoön, Kourloff, 1894; Bose, 1897; Hematozoön, Kahane, 1894; Cancriameba macroglossa, Eisen, 1900; Leydenia gemmipara, Schaudinn, 1896; Intranuclear parasite, Schuller, 1901-4.

BLASTOMYCETES.—Saccharomyces neoformans, Sanfelice, 1896; Plimmer, Leopold; Roncali, Bra; Russell's fuchsin bodies; Mucor racemosus, Schmidt, 1906.

MYCETOZOA.—Plasmodiophora brassicæ, Behla, Podwyssoski, Feinberg, Gaylord, Robertson and Wade.

SPIROCHETÆ.—Gaylord, Calkins, 1907; Cyanid-fast bodies, Robertson, 1907.

This list is of special value as showing two things—first, the enormous amount of work that has been devoted to the subject, and, second, the frailties of human judgment. Practically none of these men published their results until they were sure that they had confirmed them, and many had the advice of distinguished protozoologists. From all of these results there has come only one thing of value—namely, a healthy skepticism on the part of other workers. Almost, however, this identical situation held for syphilis until Schaudinn and Hoffman demonstrated its cause only a few years ago, and it is by no means inconceivable that some modern Pasteur will prove to us that cancer is a disease that is caused by a micro-organism.

Contagiousness.—There are certain factors that speak for the fact that cancer may be more or less contagious. These facts are:

Cancer of the thyroid gland is probably epidermic in the fish of certain hatcheries. Recent articles stating that these were not true cancer, but only adenomata, refer merely to local conditions in certain hatcheries. It must, however, be admitted that a systematic investigation should again be made in order to settle this point definitely.

Cancer seems to be more prevalent in certain localities than in others; in some it has been almost endemic for a certain length of time.

Nurses who have nursed cancerous patients for a number of years, whether or not they are related to the victim, seem to be especially liable to suffer from cancer.

Cancer is certainly inoculable, though usually within very narrow limits; mouse cancer is not inoculable from a white mouse to a gray one, so it would be unreasonable to expect human cancer to be inoculable to the lower animals. Again, this condition is somewhat similar to that pertaining in syphilis.

Sarcoma can be transmitted by a filterable virus according to a late publication by Rous and Murphy.[16]

In transplanted epithelial tumors in animals the connective tissue has been stimulated to neoplastic formation, as already mentioned earlier in this chapter.

Carcinoma or sarcoma usually develop at points of lowered resistance, so often spoken of in dermatology as precancerous dermatoses.

Malignant neoplasms in plants may be due to the *Bacterium tumefaciens,* according to the recently published researches of Erwin Smith.[17] This seems to be the most definite work so far published.

And yet it must be admitted that cancer of the penis has never been proven to cause cancer of the uterus in the wife of a patient, nor has cancer of the lip ever been shown to cause another cancer.

INCIDENTAL FACTORS.

Age.—Cancer of the skin usually occurs in those well past middle life.

Sex.—The two sexes are almost equally affected, except in cancer of the mouth, which is very rare in women.

Race.—The native American Indian rarely suffers from cancer of the skin. The negro only exceptionally suffers from basal-celled cancer, but does have the spinocelled type about as frequently as the white man. In the fifteen cases of cancer of the skin and mucous membrane that the author has recently seen among negroes there was but one rodent ulcer; all of the other lesions were microscopically proven to be of a more virulent type. The lymphomata are likewise rare.

The multiple, idiopathic, hemorrhagic sarcoma of Kaposi is most frequent in Hebrews.

Heredity.—Judging from clinical data alone, heredity seems to play no part in the production of cancer of the skin. Some of the multiple benign growths are, however, often found in members of the same family.

It would be highly improper in dealing with cancer not to speak of the important work done by Maud Slye.[18] She has shown that in mice the tendency to develop cancer is transmitted from generation to generation in exact accord with the laws of heredity, so that

[16] Rous and Murphy: Jour. Exp. Med., 1913, xvii, 219.
[17] Smith: Washington Med. Annals, 1913, xii, 1.
[18] Slye: Jour. Med. Research, 1914, 1915.

it can be bred in and out of strains of mice at will. It is not cancer itself that is transmitted, but the tendency of the cells to produce cancer under suitable conditions. She states: "The elimination, as far as possible, of all forms of overirritation of the tissues of an individual of high cancer ancestry should go far to eliminate the provocation of cancer; and the eugenic control of matings, so that cancer shall at least not be potential on both sides of the hybrid cross, ought to eventuate in a considerable decrease in the frequency of human cancer."

Trauma.—By trauma is meant not so much one injury as a chronic irritation or a series of injuries. Cancer of the skin is very apt to originate in a spot that has been more or less continuously subjected to irritation, or upon an abnormal part of the skin, such as a wart or mole. The melanotic carcinomata spring from congenital, or more rarely acquired, moles that have been irritated. The more malignant types of cutaneous carcinomata are apt to spring from the scars of old burns, or of some preexisting dermatosis.

Light.—Hyde[19] has clearly shown that those who are the most exposed to sunlight are the most apt to suffer from basal-celled carcinomata, the malignant growth usually being preceded by a keratosis. More recently Lawrence[20] has called attention to the prevalence of keratoses and cancer in the dry and sunny regions of Australia, and entirely independently reaches the same conclusions as does Hyde. It is a well-known fact that in xeroderma pigmentosum the lesions are made much worse by exposure to the actinic rays of the sun. Unna has described a condition known as "sailor's skin," in which seamen more especially, but also those exposed to much light, suffer from multiple cancers of the more benign variety. Of course, cancer is especially apt to develop upon chronic x-ray dermatoses. It may be clearly stated, therefore, that exposure to actinic rays certainly leads to the formation of cancer of the skin.

Occupation.—Schamberg[21] has recently contributed an excellent chapter to the subject of cancer due to certain occupations, especially chimney sweeps, and paraffin and tar workers. These substances undoubtedly cause keratoses upon the skin, and these keratoses may later become malignant. In addition to reporting several cases of his own, Schamberg has thoroughly reviewed the literature and collected all of the reported cases. It would seem that cancer, usually of a mild form, is very common among those forced to

[19] Hyde: Amer. Jour. Med. Scien., 1906, cxxxi, 1.
[20] Lawrence: Trans. of 7th Internat. Congr. Derm. and Syph., Rome, 1912, 1219.
[21] Schamberg: Jour. Cut. Dis., 1910, xxviii, 644.

handle the crude tar, and that in nearly every factory a number of cases can be found. The lesions are usually situated upon the hands, and are associated with a marked folliculitis. In chimney sweeps the disease generally appears upon the scrotum, due to the collection of the soot in the skin rugæ in this region, and, while at first comparatively benign, yet quite frequently leads to death. Cancer is also reported in gardeners who handle soot in the course of their work.

The etiology of cancer of the skin is still *sub judice*, but we do know that cancer frequently develops upon keratoses caused by various external irritants, such as tar, light, or the internal administration of arsenic. Also, cancer is apt to develop upon other lesions of the skin, these being fully considered in the next chapter. The work of Smith in showing that a disease in plants that is certainly analogous to cancer is due to bacteria, the work of Rous and Murphy in demonstrating that chicken sarcoma can be inoculated from a filtrate passed through a Berkfelt filter, Ehrlich's[22] demonstrations that mouse cancer is rendered more virulent by being transmitted through several generations, and Gaylord's[23] experiences with infected cages, not to mention certain of Behla's[24] statistics, would seem to show that cancer is probably due to an infecting organism of some sort. It is well known that a riotous proliferation of cells can be caused by external irritants, and the fact that cancer so frequently develops upon the site of an old injury or of a more recent break in the skin may simply mean that here is the chance for the infecting organism to gain foothold. The long periods of latency before a metastasis manifests itself is certainly in harmony with this theory. Against it speaks strongly the rarity of "cancer a deux."

[22] Ehrlich: Zeitschr. f. Aerztl. Fortbild., 1906, 7.
[23] Gaylord: Jour. Am. Med. Assn., 1907, xlviii, 15.
[24] Behla: Deut. med. Wchnschr., 1901, xxvii, 427.

CHAPTER II.

PRECANCEROUS DERMATOSES.

As Bowen[1] states in a recent article, various keratoses form the commonest cutaneous lesions that become cancerous. Certain of the soft nevi, however, especially the common pigmented moles, and scars resulting from various causes, either infectious or traumatic, are apt to become the seats of epithelial tumors, often of an extremely malignant nature.

PIGMENTED MOLES.

For many years it has been well known by dermatologists, and to a somewhat lesser extent by surgeons, that the most virulent form of skin cancer (or sarcoma)—namely, the melanotic—always has its origin in either congenital or acquired pigmented moles. In 1903, Bloodgood,[2] and a few months later Keen,[3] two eminent American surgeons, showed how frequent and fatal these growths were. They further stated that not only all acquired moles, but all congenital moles, that began to grow, that showed any signs of ulceration, or that were subject to continuous irritation, should be removed as a prophylactic measure. Unfortunately, although this point is now conceded by all surgeons and dermatologists, neither the profession at large nor the general public is as yet educated up to it, but there are many signs of an awakening.

Neither the large raised, hairy moles, nor the small hairy ones, are apt to develop into melanotic growths, and only rarely do they become the seat of basal-celled cancers. The almost flat, deeply pigmented, common moles are the dangerous ones.

Histology.—Histologically, these benign growths consist of more or less epithelial hypertrophy; beneath the rete there is a thin layer of normal corium, and then come the characteristic large nevoid cells, closely grouped together, as shown in Fig. 1. Some of the pigment is in these cells, but may also occur in the neighboring corium. There is considerable discussion as to whether these cells are of mesoblastic or epithelial origin, the weight of evidence seeming to favor the latter view. This question will be fully discussed in the chapter devoted to the malignant melanotic growths.

[1] Bowen: Jour. Cutan. Dis., 1912, xxix, 241.
[2] Bloodgood: Progressive Medicine, Dec., 1903, 149.
[3] Keen: Jour. Amer. Med. Assn., 1903.

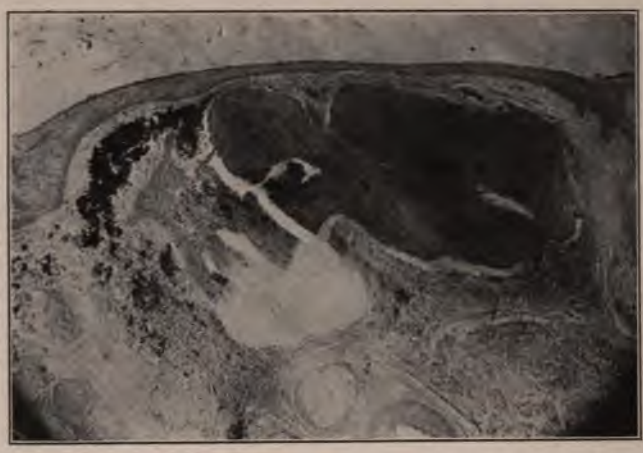

Fig. 1.—In this photomicrograph of an ordinary pigmented mole may be seen the masses of nevoid cells containing pigment, and also pigment scattered throughout the neighboring corium. There is a layer of normal corium between the rete and the underlying masses of cells. (Author's collection.)

Malignant Degeneration.—The first clinical evidences of malignancy are often very slight; there may be a slight growth or a slight ulceration, possibly followed by the development of a tumor (Fig.

Fig. 2.—The patient shown in this illustration had a common mole of the neck, which he irritated while shaving. It was removed under local anesthesia, and promptly recurred with the result shown. There were many other growths both in the skin and glands. (Heidingsfeld's collection.)

2), but the condition to be dreaded is the wonderfully rapid formation of metastases, either in the skin or in the glands or viscera. Metastasis may take place before any change is noted in the mole. Bloodgood states that the first pathological evidence of malignancy is to be found in the invasion of the corium just beneath the rete, and above the nevus, by nevoid cells.

Treatment.—When it is deemed advisable to remove a mole, it may be done by any one of several methods. Engman[4] and Bevan[5] state that the actual cautery should always be used, believing that the use of the knife or of caustics favors the dissemination of cancer cells. Bloodgood,[6] however, advocates the knife, stating that dissemination is always so rapid that the above criticisms are not pertinent. Personally, the author believes that when it is suspected that malignant change has taken place, or is about to take place, the cautery should be used, but that in removing a mole for prophylactic purposes the electric needle will suffice. Bloodgood states that he has excised a number of moles that have been treated with carbon dioxid snow by capable dermatologists, and that all of the nevoid cells were not destroyed, and hence he cannot recommend this method.

SEBORRHEIC WARTS.

Clinical Course.—These lesions, also called senile warts and seborrheic nevi, are very common on the backs and faces of elderly persons. Upon the face they usually develop upon the temples, or sides of the face, or near the midline, especially upon the nose. They develop slowly, first appearing as minute yellowish, somewhat scaly, patches, usually roughly oval in shape, and varying in length from 2 to 20 mm. A little later the follicular openings can be recognized as black spots, and still later there is the development of a thick, closely adherent black scale. At first the lesions are but little elevated above the skin level, but later become distinctly so. Itching is rare. The later course has been recently carefully studied by Sutton.[7] He concludes that there are three types of advanced lesions—namely, the keratotic, the nevoid, and the verrucose. The keratoid is usually small and is covered with a hard, dark crust. The nevoid approaches the type described by Unna, and appears as a soft, yellowish lesion, with but little horny thickening, while the verrucose lesions have a thin, yellowish crust, which when removed shows a

[4] Engman and Buhman: Medical Herald, 1913, 277.
[5] Bevan: Quoted by Bloodgood, Progressive Medicine, Dec., 1904, 175.
[6] Bloodgood: Progressive Medicine, Dec., 1904, 175.
[7] Sutton: Jour. Amer. Med. Assn., 1915.

distinctly warty or verrucose condition beneath. None of these lesions disappear spontaneously.

Pathology.—Histologically, these lesions have been studied by Pollitzer,[8] Unna,[9] Hartzell,[10] Fordyce,[11] Sutton and others. The following account is taken from Sutton's description. The keratoid variety is characterized by great corneus hypertrophy, some parakeratosis, a moderate degree of acanthosis, slight proliferative changes in the germinal layer, with some flattening of the papillary bodies.

Fig. 3.—This illustration shows a fungous cancer, which sprang from a seborrheic keratosis, similar to the ones upon the cheek and nose. (Sutton's collection.)

The sweat ducts are dilated and cysts may be formed. The sebaceous glands are normal, but contain much free fat. The blood vessels of the corium are dilated, and there is some infiltration of the subpapillary portion, with small round and fixed tissue cells.

The nevoid type showed changes similar to those described by Unna in his "nevus seborrheoicus"—that is, but little change in the epithelium, although there is some slight parakeratosis, but a marked

[8] Pollitzer: Monatshefte f. prakt. Dermat., 1890, xi, 145.
[9] Unna: Histopathology of the Skin (Walker's translation).
[10] Hartzell: Jour. Cutan. Dis., 1903.
[11] Fordyce: Jour. Amer. Med. Assn., 1910, lv, 1624.

increase of pigmentation in the derma, together with dilatation of the blood vessels, and a heavy infiltrate, with round or polygonal cells that resemble nevoid cells. The glandular elements are but little altered.

The verrucose form is distinguished by considerable hyperakeratosis, very pronounced acanthosis, active proliferative changes in the germinal layer and also at times in other portions of the rete, and most especially by great papillary hypertrophy. The cutis shows changes of a subacute inflammatory nature.

Malignant Degeneration.—Basal-celled cancers are very prone to develop upon these lesions when they are situated upon the face, and occasionally a prickle-celled cancer develops in this situation. When these lesions develop upon the hands, prickle-celled cancer is a common result. The first malignant change noted is a slight ulceration, accompanied by a serous discharge. This ulceration slowly spreads and there is an increase in the induration. It is highly probable that nearly five percent of all these keratoses, especially those of the keratoid variety, terminate in carcinoma.

Treatment.—In the early stage these growths are easy to remove. The crust can be removed by an ointment of salicylic acid, and carbon dioxide snow applied to the base for thirty seconds with firm pressure. Another way is to curette off the scale and then use silver nitrate. When a heavy crust has once formed, treatment must be more radical, and the growth should either be excised or treated with the actual or electric cautery. If there is any suspicion of malignancy, operation must be extensive.

SIMPLE KERATOSIS.

Clinical Course.—Solitary patches of keratosis may develop in the elderly, usually upon the face or the hands (Fig. 4). They start as papules from 1 to 3 mm. in diameter, and are of great surface hardness, due to a piling up of the horny layer. This thickening of the keratin soon becomes black in color. The crust is very adherent, and usually becomes detached only once or twice a year. They rarely grow to more than 5 mm. in diameter, and are sometimes multiple, although it is rare to find more than three or four such lesions in any one person.

Histology.—Histologically, the changes are very similar to those described as occurring in senile warts, but there are no signs of an undue amount of fat being present.

Malignant Degeneration.—These patches may become malignant, the first change noted being ulceration and serous discharge.

Fig. 4.—This patient, a very old man, has had this horny growth upon his hand for about a year. It was cured by excision. (Author's collection.)

Treatment.—Treatment is identical with that described under senile warts.

ARSENICAL KERATOSES.

That arsenic may cause keratoses is not a particularly unfamiliar fact, but it has been within the past few years that it has become generally recognized that the internal administration of that drug can cause keratoses that may eventuate in carcinomata. These lesions have been carefully studied by Hartzell,[12] Schamberg,[13] and Fordyce,[14] all of whom agree on the essential points. Arsenic must be administered over a considerable length of time, and in fairly large amounts. Typical keratoses appear which have a histology that is essentially the same as those already described. The cancers are prickle-celled ones.

[12] Hartzell: Amer. Jour. Med. Scien., 1897, cxviii, 205.
[13] Schamberg: Jour. Cutan. Dis., 1907, xxv, 26.
[14] Fordyce: Amer. Jour. Med. Scien., 1910, lv, 1624.

KERATOSIS FOLLICULARIS.

Wende[15] has reported a remarkable case where the keratotic lesions of Darier's disease become carcinomatous. It is only surprising that this condition has not occurred more frequently.

CUTANEOUS HORN.

It is generally known that cutaneous horns often become malignant, the change taking place at the base, and being evidenced by ulceration, secretion, and induration (Fig. 5).

Fig. 5.—A cutaneous horn first arose upon some senile warts. When the picture was taken, there was infiltration and ulceration at the base of the growth. Microscopical examination showed the presence of early cancer. (Heidingsfeld's collection.)

CANCER OF PARAFFIN WORKERS.

Schamberg[16] has recently published a most complete paper on the prevalence of cancer in tar workers, paraffin workers, and chimney

[15] Wende: Jour. Cutan. Dis., 1908, xxvi, 531.
[16] Schamberg: Jour. Cutan. Dis., 1910, xxviii, 644.

sweeps. The crude petroleum has a particularly irritating effect upon the skin, especially around the hair follicles. These are found to be filled with dark, spiny plugs. Not infrequently keratoses form, and later cancerous changes occur. In chimney sweeps the scrotum is usually affected, due to the collection of soot in the rugæ of the skin. This frequently results in death from lymphatic involvement. Cancer has also been recorded as occurring in gardeners who use soot in the course of their work.

XERODERMA PIGMENTOSUM.

Unna's description of the clinical course of this disease still remains classical, and but little has been added. He states that this disease was first recognized by Rüder and by Kaposi.

Clinical Course.—It usually begins with an inflammatory hyperemia and a freckle-like condition, the freckles doubtless being protective in intent. As a general rule, only the exposed parts of the skin are involved at first, but later in the course of the disease the whole skin may be involved. The first changes are noticed between the ages of five and ten months, and progress but slowly. At a little later date it is noted that there are atrophic areas in the skin, and also venous telangiectases (Fig. 6). Between the ages of fifteen and twenty years keratoses usually manifest themselves, and from the earliest stages the skin is remarkably rough and dry. The eyes are exceedingly sensitive to light, and the patient hangs his head and keeps the eyes closed when the illumination is at all bright. At about the age of twenty some of the keratotic patches become malignant, and the growth of these carcinomata is usually slow and typical of rodent ulcers. Occasionally the course of the disease is much more rapid; in the patient illustrated in Fig. 7 large cancers had developed at the age of fourteen.

Pathology.—Histologically, the lesions have been studied by Unna, Kaposi,[17] Fordyce,[18] and others. The very earliest lesions have not as yet been sufficiently studied, but the second stage—that is, where there is a marked increase in the amount of pigment—is well known. The basal layer of the rete contains an abnormal amount of pigment, and the rete as a whole is thinned and atrophic. The papillæ are widened by congestion. The changes in the corium are found over the entire skin. The varices do not form under the pigment, but only where this is lacking. Unna states that in the areas

[17] Kaposi: Twentieth Century Practice of Medicine, v.
[18] Fordyce: Jour. Amer. Med. Assn., 1910, lv, 1624.

of excessive pigmentation the pigment is found not only in the rete, but also in the papillary spaces, partly in the lymph spaces and partly in the hypertrophic spindle cells. Scattered clumps are also found in the upper prickle layer.

Fig. 6.—This boy, aged 12, had suffered from freckles since he was 2 years old. Atrophic areas, areas of pigmentation, and a keratotic lesion upon h's neck can be seen. The condition is one of xeroderma p'gmentosum. (Case in the Johns Hopkins Hospital.)

In the third stage there exists great thickening of the horny layer, so as to form horny warts or keratoses, beneath which the rete is deformed in spaces corresponding to the black areas. In the lower prickle layer the prickles are lost, and the cells consequently are misshapen, and there is considerable intracellular edema. In the rete are masses of closely packed epithelial cells loaded with pigment. At times collections of nevoid cells are found in the upper portion of the corium, all loaded with pigment. The white sclerotic spots are due to an obliteration of the capillaries, caused by the sclerosis and hypertrophy of the connective tissue of the corium. There is usually some round-celled infiltration around the basal layer. The cancers developing in these patches are typical basal-celled carcinomata, showing, however, an increase in pigment.

Fig. 7.—The same patient illustrated in Fig. 6. Had a number of well-developed cancers arising from the keratoses. Microscopically, they were shown to be basal-celled. The condition is xeroderma pigmentosum. (Case in the Johns Hopkins Hospital.)

The condition is believed to be due to a congenital lack of resistance to the rays of the sun, and the increased pigmentation, as well as the early erythema, is an attempt on the part of the body to protect itself against the actinic rays. It is not unusual to find a number of children in the same family similarly affected with this disease.

Treatment.—The prognosis is always bad, the patients may be relieved for a short time, but eventually death results from carcinomatosis of the skin, occasionally complicated by visceral metastases.

Treatment is unsatisfactory, and simply consists in delaying the fatal termination. The patients should be exposed to sunlight as little as possible, and it would be better if the windows of the room in which they are kept were of red glass, so as to filter out the actinic rays. In addition to this, the exposed portions of the body should either be covered by a mask or by a red ointment or lotion, calamine being fairly satisfactory for this purpose. Whenever a carcinoma appears, it should be radically removed at once, or, better yet, the keratoses should be excised as soon as they appear. In other respects the treatment is purely symptomatic, treating symptoms as they develop.

SAILOR'S SKIN.

This condition was originally described by Unna as occurring in sailors who were much exposed to weather and sun. The condition, as will be shown later, is not confined to seafaring men, but also occurs in farmers and those who are exposed to a dry climate and excessive actinic rays. In both of these groups of cases there is an acquired hypersusceptibility to actinic rays, as opposed to the congenital intolerance that appears to be the basis of xeroderma pigmentosum.

There first appears upon the exposed parts a diffuse cyanotic redness. Pigment spots soon appear, but the areas between these "freckles" may or may not lose their pigment. Telangiectases appear, and the skin becomes dry and hard, and keratoses usually result. This condition may last for years, but usually there develop basal-celled carcinomata, that run the clinical course of rodent ulcers.

When this condition begins to develop, the patient should give up an out-of-door life, or at least protect himself from light. In the later stages the treatment consists of the surgical removal of the growths.

FARMER'S CANCER.

The condition described by Unna as peculiar to seamen is also found in those who are much exposed to the sunlight, especially where the air is very dry. As it is fairly common in the western part of the United States among those following agricultural pursuits, it has been aptly named "farmer's cancer." The condition commences with a deep bronzing of the skin, later the cutaneous covering becomes dry and rough and minute keratoses develop.

Hyde[19] has thoroughly considered this type of dermatosis, showing how frequently rodent ulcers develop upon these keratotic patches. More recently Lawrence[20] has called particular attention to the prevalence of this disease in Australia. Lawrence states that out of 6,000 consecutive cases at his clinic 1.8 percent, or 108 cases, showed this condition, a figure greatly in excess of the prevalence of rodent ulcers at the European skin clinics. He attributes the condition to the great amount of sunshine and the low relative humidity of the atmosphere.

The treatment is the same as for "sailor's skin."

X-RAY DERMATITIS.[21]

Clinical Course.—This sad condition was much more frequent in the early days of x-ray therapy than it is at present. In those days the operators took no precautions to shield either themselves or patients from long continued exposure to the soft rays, and the result was that there were very many sufferers. The condition is in every way analogous to the conditions just described, and is undoubtedly caused by the actinic rays of the Roentgen tube. The backs of the hands are well known to be the most susceptible portions of the body, and here it is that this condition is most often seen.

Again, we see the developing of an excess of pigment, usually in freckle-like spots, then there appear superficial telangiectases; the skin becomes dry and rough, and loses its secretions, and the hairs fall out. The nails frequently become stunted and roughened. Small horny growths appear, usually upon the site of the freckles. These later develop into either ulcers or carcinomata. The cancers may be either of the basal-celled or the prickle-celled type, or a mixture of the two. In the case of the squamous-celled cancers the spread is usually rather rapid, and local removal nearly always followed by recurrence, and at times by metastases. Even the basal-celled carcinomata usually grow fairly fast.

Pathology.—Pathologically it is conceded that the first changes manifest themselves in the corium and not in the epithelium. The sweat and sebaceous glands become atrophied, the blood vessels are dilated, and there are signs of an inflammatory process, with round-celled infiltration.

[19] Hyde: Amer. Jour. Med. Sc., 1906, cxxxi, 1.

[20] Lawrence: Trans. 7th Internat. Congress Dermat. and Syphil., Rome, 1912, 1219.

[21] Porter and White: Ann. of Surg., 1907, xlvi, 649.

Treatment.—In dealing with this very serious malady an ounce of prevention is worth many pounds of cure, and fortunately this fact is now recognized by every x-ray worker. The hands of the physician should never be exposed to the emanations of the tube. Prevention is now thoroughly dealt with in all of the excellent works now existing on the subject of the practical use of this therapeutic remedy. The callosities should be removed either by the use of the knife or by the cautery and curette. To the author it seems illogical to use either the Roentgen tube or radium, for he cannot help feeling that there is grave danger of thereby aggravating the condition, recalling that the trouble is caused by light. Whenever an ulcer appears, it should be excised and skin-grafted, and cancers should be excised with an ample margin. If they are of the spinocell type, amputation and removal of the neighborly glands should be seriously considered.

PAGET'S DISEASE.

Paget's disease is often considered as a precancerous condition, but, as there is still dispute as to whether the cutaneous lesions may not be secondary to the cancerous changes the writer has felt it best to deal with this subject in a special chapter.

MARJOLIN'S ULCER.

Cancer frequently develops upon the scars of various dermatoses. Most prominent of these is the scar resulting from ordinary burns of the third degree. Cancer originating in such lesions is commonly called *Marjolin's ulcer*. The first manifestation is almost invariably a superficial ulcer, with a considerable amount of rather foul discharge. A fungous overgrowth often results, with great induration around the edges. At other times there is simply a deep ulcer, accompanied by induration. Cancers of this type are usually of the spinous-celled variety, necessitating wide local removal, and enucleation of the draining lymphatic glands. In severe cases situated upon the limbs amputation is usually necessary.

LUPUS VULGARIS.

Lupus vulgaris of many years' duration is not infrequently complicated by cancer. Sequeira[22] has recently published an excellent article on the prevalence of malignant change in lupus, and has reported a number of very interesting cases. He concludes that the

[22] Sequeira: Brit. Jour. Dermat., 1908, xx, 40.

cancerous degeneration develops only in long standing cases, and usually in persons about the prime of life. It is usually stated that about 2 percent of all cases of lupus become cancerous. Contrary to the statement of most observers, Sequeira believes that this change is more common in men than in women. The change takes place more frequently upon the face than elsewhere (Fig. 8). It is still questionable whether x-ray treatment of the lupus has been responsible for the malignant change, but apparently cancer is no more common in the cases treated by the x-ray than in the cases

Fig. 8.—This woman had suffered from lupus vulgaris for years. A deep spinocelled cancer has developed and is invading her orbit. (Heidingsfeld's collection.)

treated by some of the older methods. At the same time it must be remembered that it is only within a comparatively few years that the ray has been persistently used in lupus, so the future may hold many such cases in store for us. The tumors are almost invariably of the prickle-cell type, and spread rapidly and frequently metastasize. Radical operation is indicated in all cases. Local removal and radiation of the base of the ulcer is not sufficient; it may cure a few cases, but cannot give good results when tested on many patients.

LEG ULCERS.

Chronic leg ulcers rarely become cancerous. Both Bloodgood[23] and Gottheil[24] have noted this, the former having seen but three cases, and the latter having been able to collect but ten cases from the literature. Most dermatologists and surgeons express surprise that such a change does not take place more frequently, but to the author it does not seem surprising when one considers that cancer prefers to originate from a dry sore and not from a moist one. In common with most carcinomata of the extremities, these growths are usually of the spinous-celled type and hence are very malignant. Operation should consist of wide local removal, the glands likewise being taken out. Amputation is frequently necessary. In the case illustrated in Fig. 30 the growth was curetted and excised, and thoroughly cauterized with acid nitrate of mercury, and has escaped recurrence for three years.

LUPUS ERYTHEMATOSUS.

Lupus erythematosus scars occasionally become the seat of skin cancers. Dubreuilh and Petges[25] have collected all of the cases reported in addition to recording two of their own. In practically all of the patients the lupus had existed for many years, and the neoplasms originated upon the scar tissue. So far as can be judged from the rapidity of their growth, they were of the spinous-celled variety. More recently Janeway[26] has recorded another case occurring after the use of carbon dioxide snow. Gottheil, in discussing this case, held that previous x-ray treatment was probably the true factor.

BLASTOMYCOSIS.

That the *lesions of blastomycosis* may become cancerous has been shown by Bloodgood[27] in a case that the writer was fortunate enough to see with him.

SYPHILIS.

Syphilitic ulcers are often referred to as undergoing malignant degeneration, but the condition is certainly unusual. The change may take place either in an ulcer or in the scar produced by such

[23] Bloodgood: Progressive Medicine, Dec., 1904.
[24] Gottheil: Jour. Amer. Med. Assn., 1912, lvix, 14.
[25] Dubreuilh and Petges: Ann. de dermat. et de syphil., 1909, x, 106.
[26] Janeway: Jour. Cutan. Dis., 1910, xxviii, 140.
[27] Bloodgood: Progressive Medicine, Dec., 1907.

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an ulcer, usually the latter. In the former instance it is noted that the granulation tissue becomes raised at some point, and that it bleeds very readily. The tissue is friable, and is slightly paler than the rest of the granulations. Induration may be felt around the edges. The further course shows either a deeply eating ulcer or a fungous growth, or a combination of the two. These lesions are usually of the more malignant type, and hence demand extensive operative interference.

INFLAMMATORY DERMATOSES.

Eczema, lichen planus and psoriasis (Hartzell,[28] Bloodgood[29]) occasionally give rise to cancer of the skin, but in the vast majority of the cases reported it is probable that either arsenic or x-ray was the true cause.

SINUSES.

Bloodgood frequently refers to *sinuses and fistulas* as being the starting points of epithelial neoplasms, but admits that, when one considers the frequency of such conditions, the subsequent development of cancer is rare. He also mentions one case of malignant change in a bedsore.

WENS.

Wens may serve as the starting points of cancer according to Bloodgood,[30] who has recorded three cases where malignant change took place in the wall.

NEVI.

Vascular or *pigmented nevi* not infrequently become the starting points of sarcomata, and rarely of carcinomata of the skin.

PAPILLOMAS.

The *fibro-epitheliomata of the skin,* commonly called papillomas, frequently give rise to either basal- or prickle-celled cancers, especially when they are subject to chronic irritation.

[28] Hartzell: Amer. Jour. Med. Scien., 1899.
[29] Bloodgood: Progressive Medicine, Dec., 1907.
[30] Bloodgood: Progressive Medicine, Dec., 1913.

CONCLUSIONS.

In a recent review of the literature Sutton[31] points out that the line separating malignant from benign epithelial growths of the skin is often a very obscure one, and that tumors of the rodent ulcer type may originate in the lesions of the so-called multiple benign cystic epitheliomata. He does not, however, agree with Heidingsfeld,[32] who believes that all growths of this type are premalignant in character.

Both Montgomery[33] and Sutton[34] have shown how frequently cancer of the lip starts in seborrheic patches, and for years it has been known that cancer of the tongue frequently originates in syphilitic lesions as well as in leukoplakia.

Bloodgood[35] states that every case of cancer of the skin of which he has a complete record originated from some abnormality of the skin, and not from normal epidermis. He also states that out of forty cases of cutaneous sarcoma, thirty-two originated from distinct skin lesions, usually the scars of burns. These statements show that, if all apparently harmless cutaneous growths were removed, we should have fewer cancers. It also means that we should do our best to promptly heal all lesions, and not allow them to drag along.

[31] Sutton: Amer. Jour. Med. Scien., 1913, cxlv, 819.
[32] Heidingsfeld: Jour. Amer. Med. Assn., 1912, lvix, 256.
[33] Montgomery: Jour. Cutan. Dis., 1913, xxx, 82.
[34] Sutton: Jour. Amer. Med. Assn., 1913, lx, 1774.
[35] Bloodgood: Progressive Medicine, Dec., 1912.

CHAPTER III.

EPITHELIAL WARTS.

There are, of course, two varieties of epithelial warts—the benign and the malignant.

BENIGN WARTS.

Both clinically and pathologically the benign warts may be divided into four main classes, each of which contains subdivisions.

A. Keratomata.
   a. Simple keratoma.
   b. Clavus.
   c. Callus.
   d. Cutaneous horn.
   e. Angiokeratoma.

B. Acanthoma (spino-celled tumor).
   a. Molluscum contagiosum.

C. Mixed-celled tumors (reteomata).
   a. Verruca vulgaris.
   b. Verruca digitata.
   c. Verruca filiformis.
   d. Condyloma acuminata.
   e. Semiglobular wart.
   f. Pedunculated fibroreteoma.
   g. Seborrheic warts.
   h. Acanthosis nigricans.

D. Basal-celled warts.
   a. Nevus-like warts.
   b. Multiple benign cystic epithelioma.

In addition to the true wart-like growths, certain infectious diseases of the skin frequently assume a papillomatous overgrowth, consisting of hypertrophied epithelium. Among these may be mentioned lupus vulgaris, and various other forms of tuberculosis of the skin, frambesiform syphilis, blastomycosis, yaws, and occasionally eczema.

The different growths mentioned above form a veritable hodge-

podge, a set of tumors very different in their clinical manifestations as well as in their etiology. They are here grouped together simply because they all form a more or less wart-like projection above the level of the skin and all show epithelial proliferation.

Keratomata.—Of the true keratomata there are several varieties, all sufficiently well described in the text-books on dermatology.[1]

By *simple keratoma* the author has reference to the single or multiple keratosis already described on page 39, and here referred to simply for the sake of completeness.

Clavus or *corn* is too well known to need any detailed clinical description. Pathologically, it is a true keratoma of wedge-like shape, with the apex pointing downward.

The *simple callosity* is likewise too well known to merit comment; it is a diffuse keratoma, due to a combination of pressure and friction.

The *cutaneous horn* has only an outward resemblance to the horns of animals, but has not their hardness, being about equal in consistency to the normal nail. The length varies from 5 mm. to 10 or 15 cm. They may grow singly or in groups; in the latter case there is usually one large one surrounded by smaller ones. The point of origin is often a keratosis, or a fibroma, but usually a seborrheic patch. They grow out from and are attached by the horny layer that reaches down between the greatly elongated papillæ.

Angiokeratoma were first described by Mibelli.[2] They appear on the hands or feet of young persons on a basis of local asphyxia, and consist of capillary ectases, with a surmounting keratoma. They first appear as red spots that disappear under pressure, next as permanent capillary dilatation, and finally the keratoma develops.

Acanthoma (Prickle-celled Tumors).—The *molluscum contagiosum* is the only true tumor consisting almost entirely of prickle cells. Clinically, they are sharply-defined, single, semiglobular tumors, of a translucent appearance, and showing a central depression. They vary in size from 2 to 6 mm., and usually appear upon the faces of children, and the genitalia of adults. They are undoubtedly spread by autoinoculation and contagion, and they frequently appear in small epidemics, either in schools or among the patrons of the so-called Turkish baths. Upon firm pressure a colloid-like material may be expressed from these growths. Histologically, there is a marked

[1] Crocker: Diseases of the Skin, 3d ed., Phila., 1905.
Hyde: Diseases of the Skin, 8th ed., Phila., 1909.
Pusey: Principles and Practice of Dermatology, New York, 1907.
Stelwagon: Diseases of the Skin, 6th ed., Phila., 1910.

[2] Mibelli: Inter. Atlas Rare Skin Dis., vii, 1889.

amount of acanthoid tissue that has undergone colloid degeneration (Fig. 9).

Mixed-celled Tumors (Reteomata).—*Verruca vulgaris* is the common wart so often found upon the hands and scalp of the young. At times it occurs upon the soles of the feet, then causing a very painful affliction. That the common wart is infectious is proven by the experiments of Jadassohn[3] and others, all well described in Stelwagon. It is so well known that no description is necessary; suffice it to say that the so-called seeds are simply particles of dirt that have gotten down between the elongated intrapapillary spaces.

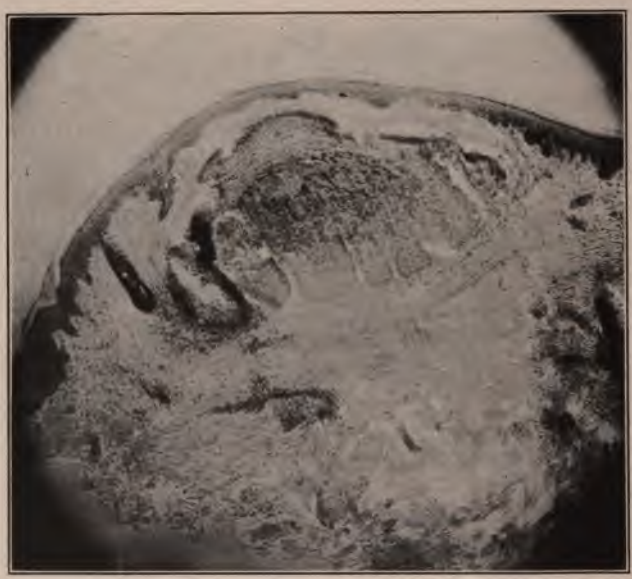

Fig. 9.—Histologically, the lesions of molluscum contagiosum consist of a pure growth of spinous cells, which have undergone degeneration. (Author's collection.)

Histologically, the papillæ are elongated, and the prickle, basal and horny layers all hypertrophied.

The *digitate wart,* or *verruca digitata,* is simply a subvariety of the preceding, the projections being very long, and are most commonly found upon the scalp.

The so-called *filiform warts* are most common upon the neck, often appearing in great numbers at the same time; fifty or even a hundred may develop within a week. They usually arise from the

[3] Jadassohn: Verhandl. d. 5ten Deutsch. Dermat. Gesselsch., 1895-96, 497.

neighborhood of the hair follicles, and are undoubtedly infectious, for, if only one be left behind, many more will usually appear. Histologically, there is proliferation of all the layers of the epithelium arranged around an increased amount of fibrous tissue.

The *acuminate condylomata,* or *venereal* warts, occur around the glans penis of men and the labia of women, and are directly due to irritating discharges, especially of gonorrhea or chancroid, much more rarely of syphilis. A typical growth resembles a cock's comb, is bright red in color, and has numerous sharp projections. Histologically, there is hypertrophy of the prickle and basal layers of the rete, and to some extent of the fibrous tissue.

The *semiglobular warts* are very common upon the faces of women, and to a somewhat less extent of men, and occasionally occur elsewhere, rarely upon the mucous membranes. Their diameter varies from 2 to 10 or 12 mm., and they are very firm in consistency. Occasionally there may be a tuft of hair at the top. They persist throughout life, with very little tendency toward malignant change, unless subject to chronic irritation. Histologically, there is proliferation not only of the fibrous tissue, but also of the prickle and basal cells.

Another common variety of mixed-celled wart is the *pedunculated* one, which is usually found upon the back, and varies in size from 5 mm. to 5 cm. in diameter. The surface is thrown into many lobulations. Histologically, the tumor consists largely of an overgrowth of fibrous tissue, but there is also an excess of the layers constituting the rete. These tumors only rarely become malignant.

The *seborrheic warts* have already been discussed in the preceding chapter.

Acanthosis nigricans is thoroughly treated in Stelwagon's book, and a complete bibliography is given. The following description is from his article.

The cutaneous lesions consist of a more or less diffuse pigmentation, that varies in color. In the flexures most especially, but to a slightly less extent over the rest of the body, the skin assumes a papillomatous overgrowth. The neck, face, lips, and mouth are also apt to share in this hypertrophy. Rarely these may degenerate into cutaneous cancers. Couillaud has come to the following conclusions: "The disease is a syndrome dependent upon abdominal carcinosis and characterized (1) from a clinical viewpoint by (a) a papillary hypertrophy and a cutaneous pigmentation having an essentially regional character; (b) a papillary hypertrophy of the mucous membrane; (c) a dystrophy of the hair and nails; (d) absence of des-

quamation; (e) existence of a cachexia; (2) from a pathologic standpoint by a carcinomatous degeneration of the abdominal organs; (3) histologically by lesions of hypertrophy and pigmentation in the rete and corium."

Whenever such a condition is present, even if there be as yet no symptoms of abdominal cancer, an abdominal operation should be performed, for there may be some hope of saving life by so doing.

Basal-celled Warts.—The pure basal-celled warts are not so well known, generally being confused with either pigmented moles or with the pigmented nevi. They have been studied by Gilchrist[4] and Bloodgood,[5] who have shown that their cells are typical basal cells, usually connected at some point with the basal layer of the rete. They do not have the larger size of the nevoid cells.

The *multiple benign cystic epitheliomata* probably belong in this group. A full discussion of them will be found in a later chapter.

Treatment.—These growths can be effectually treated in many different ways; the pedunculated ones can be snipped off with a pair of scissors, and the base cauterized with any good cauterizing agent, preferably the actual cautery.

The small soft growths can be treated with carbon dioxide snow, or, better, the electric needle, by any one of the chemical caustics, or by excision. In any of the growths where there is a marked excess of horny tissue, none of the caustic agents should be used, for only disappointment will result. The growths are better treated by the curette first and a caustic second. Even without local anesthesia there is but little pain to curettage. Of course, excision can always be resorted to, but, except in the hands of the expert surgeon, the scar is not as satisfactory as that resulting from one of the other methods. With an expert operator, excision, with a fine linear scar, is the method of choice. Fulguration is painful, useless in horny growths, and not as satisfactory as some of the other caustics. The x-ray should not be used, as quicker and less dangerous methods are always at hand.

MALIGNANT CUTANEOUS WARTS.

There are two varieties of malignant skin warts—the prickle- and the basal-celled. There is still a question as to whether the cancerous growths are malignant from the start, or whether they represent malignant degenerations of the benign variety. Borst[6] main-

[4] Gilchrist: Jour. Cut. and Gen. Urin. Dis., 1899.
[5] Bloodgood: Progressive Medicine, Dec., 1904.
[6] Borst: Die Lehre v. d. Geschwülsten, Wiesbaden, 1902.

tains that the type is determined from the very earliest genesis of the tumor. Of each class there are two subvarieties—one in which the surface is papillomatous, and the other in which it is covered by a horny crust. Both varieties are comparatively rare, and are more frequently seen by the surgeon than by the dermatologist; the prickle-celled tumors are more frequently encountered than the basal-celled neoplasms.

Prickle-celled Warts.—In his first series of 468 epithelial tumors, Bloodgood saw twenty-four malignant warts, some of which were distinct papillary epithelial growths, others resembling the verruca senilis, and still others presenting ulcerating or fungous surfaces at the edge of the growth. The most common situation was upon the lips or the face, but there were several cases upon both the tongue and the penis. In only one instance was there metastasis, and that in the case of a tumor of the chest wall. This is, perhaps, the only class of spinous-celled tumors in which a radical operation is not demanded. If the cases are seen before there is any infiltration at the base, wide local excision will suffice; but if there is basal infiltration, the neighboring lymphatic glands should be removed. At times local infection will give basal infiltration, so that, if there be any question, the surgeon may try the use of a mild antiseptic ointment for a few days, and, if the infiltration disappears, then a radical operation need not be done. In this class of tumors removal with the knife is the proper treatment. Pusey, it is true, has had excellent permanent results with the x-ray, but the majority of operators have not been so successful. In tumors of the tongue, Bloodgood considers that a radical operation should always be performed, and the same is probably true of the penis.

Basal-celled Warts.—*Malignant basal-celled warts* are very rare. Bloodgood reports one occurring upon a man sixty-seven years old. The wart, which first resembled a "pimple," had been present two years, and had often bled because of ulceration. Microscopically, the growth consisted entirely of basal cells arranged in tubular-like growths. There was no recurrence on removal. This class of tumors can be treated just as are rodent ulcers, and the results should always be satisfactory.

In diagnosing a benign from a malignant wart, the first thing felt for should be basal induration; secondly, persistent surface ulceration. The diagnosis should usually be made by the naked eye at the time of operation, the surgeon sectioning the tumor and looking for the fine white downgrowths indicating alveoli filled with cancer cells. If there be any doubt, either a frozen section should be

studied before further operation is done, or sections can be hardened and cut in the usual way, and, if necessary, operation completed at a later date.

In obtaining material for sections it is best to employ an electric cautery, excising the tissue exactly as with a knife, but giving a wider margin, inasmuch as the heat ruins much of the tissue with which it comes in contact. Frozen sections cannot be unreservedly advocated, inasmuch as it is very difficult to produce thin, well stained specimens, and hence a proper diagnosis may be clouded rather than assisted.

It is probable that the majority of malignant warts can be cured by means of proper radiation, although at the present time there are absolutely no statistics upon which to base this opinion. The lack of deep infiltration should make these tumors ideal subjects for properly administered x-rays.

CHAPTER IV.

BASAL-CELLED CARCINOMATA.

The differentiation of the basal-celled group of tumors from the other epithelial neoplasms is really due to the excellent work of Krompecher,[1] and in America the attention of both dermatologists and surgeons has been especially called to these growths by the publications of Bloodgood.[2]

This very large and important group of tumors embraces the typical Jacob's ulcers of the English author as well as of Unna, the

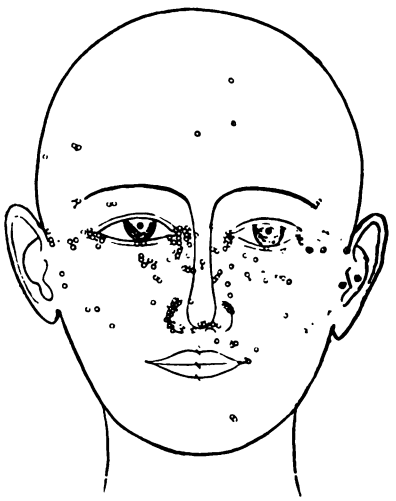

Fig. 10.—Diagram of the sites of origin of 220 cases of basal-celled cancer. (After Sequeira.)

cancroid of the early writers, and the rodent ulcers of the surgeons and dermatologists. Owing to the varying clinical and pathological pictures presented by these tumors, they have been much confused by most writers, many men not recognizing that the histological picture might vary, not only in different stages of the same growth, but also in sections taken from different parts at the same time. Some English authors have even gone so far as to speak of

[1] Krompecher: Der Basalzellenkrebs, Jena, 1903.

[2] Bloodgood: Progressive Medicine, Dec., 1904.

a rodent ulcer becoming malignant, when in reality the basal cells were simply invading the tissue in a slightly different way.

Krompecher has shown that even the glandular tumors may have a different picture and run a different course, according to which layer of the glandular epithelium from which they arise, but this need not now concern us, though it does seem wise to point out the analogy.

Occurrence.—These tumors are usually situated upon the face, especially upon the nose, eyelids, and median portions of the cheek, but may occur upon any other part of the face, or upon the back or shoulders. They are extremely rare upon the limbs. Sequeira's[3] composite illustration shows very clearly where they usually arise

Fig. 11.—This illustration shows basal-celled carcinomata arising from different portions of the rete. Serial sections showed that there was no connection between the various growths. (Gilchrist's case.)

(Fig. 10). They very rarely originate in people under thirty years of age, and are most common in the decade between forty and fifty.

It is usually stated that males are much more frequently affected than are women, some authors even stating that 90 percent of the cases occur in men and the majority believing that at least 75 percent of the patients are of the male sex. Neither Krompecher's nor the author's own statistics would seem to bear out this assumption, for Krompecher records nine in men and eight in women, and the author's figures give thirty-one in men and twenty-four in women.

Pathology.—The neoplasms spring from the basal layer of the

[3] Sequeira: Brit. Jour. Dermat., 1913, xxv, 172.

epithelium. Not infrequently they are multiple, especially in the type springing from seborrheic warts. Petersen[4] has demonstrated that the growths may have a multicentric origin. In a recent case from the Johns Hopkins Dermatological Clinic it could be clearly shown that in one nodule there were a number of separate and distinct places where malignant proliferation was beginning (Fig. 11). The whole growth was sectioned, and these small nodules had no connection with each other. From this section it was possible to demonstrate the very earliest changes, photographs of which are here

Fig. 12.—The earliest lesion of cancer is a downgrowth of the epithelium. Some of the prickle cells have lost their nuclei. There is very little infiltration of the surrounding corium. (Gilchrist's case.)

reproduced. The first change noted is an unduly long downward growth of the intrapapillary process (Fig. 12). There is some degeneration of the rete, and many of the prickle cells have lost their nuclei. There is a slight invasion of the rete by round cells and fixed tissue cells; the subpapillary portion of the corium shows a slight increase in these same cells, and the blood vessels are dilated. The second stage (Fig. 13) shows a clubbing of this downward growth; the basal cells have begun to proliferate, and the death of the cell nuclei is very apparent. The fibrous tissue of the corium shows some signs of compression, and there is an increase in small

[4] Petersen: Beitrage z. clin. Chir., 1902, xxxii, 543.

round and fixed tissue cells, some of which have invaded the rete. In the third stage (Fig. 14) the cancerous lesion is distinctly semi-

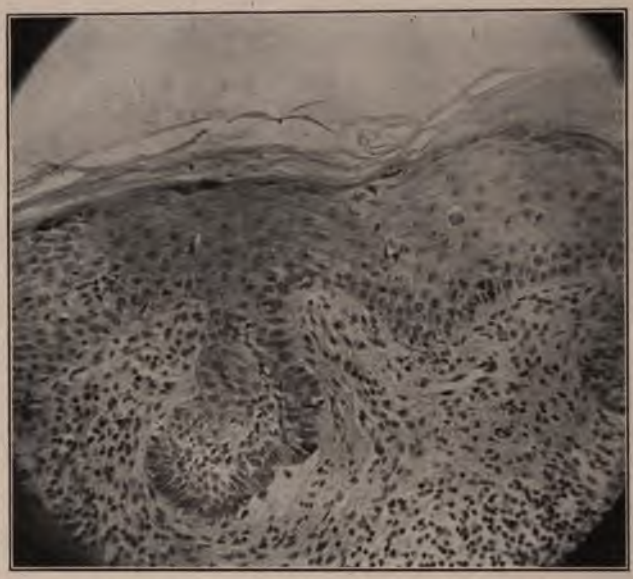

Fig. 13.—The second change in a developing basal-celled cancer is a clubbing of the downgrowth shown in Fig. 12. The basal cells are beginning to proliferate, and degenerative changes may be plainly distinguished in the spinous cells. (Gilchrist's case.)

Fig. 14.—The downgrowth contracts, so that a solid mass of basal cells is formed. (Gilchrist's case.)

globular in shape, due entirely to a proliferation of the basal cells, there may or may not be infiltration of the corium by inflammatory

cells, and the death of the nuclei of the prickle cells can be clearly seen. Some nuclei can be distinguished lying in vacuoles, either within or without the cells. In the fourth stage (Fig. 15) the basal-celled growth has invaded the rete, so that surface ulceration has taken place. At a later period the basal membrane is broken through, and the invasion of the corium begins.

After the invasion begins, the pathological picture varies. At first there are solid masses of the deeply-staining basal cells (Fig. 16), the *Carcinoma basocellulare solidum* of Krompecher and Bloodgood. The solid masses do not, however, long remain so, for they either degenerate in the center, forming cysts, or else arrange them-

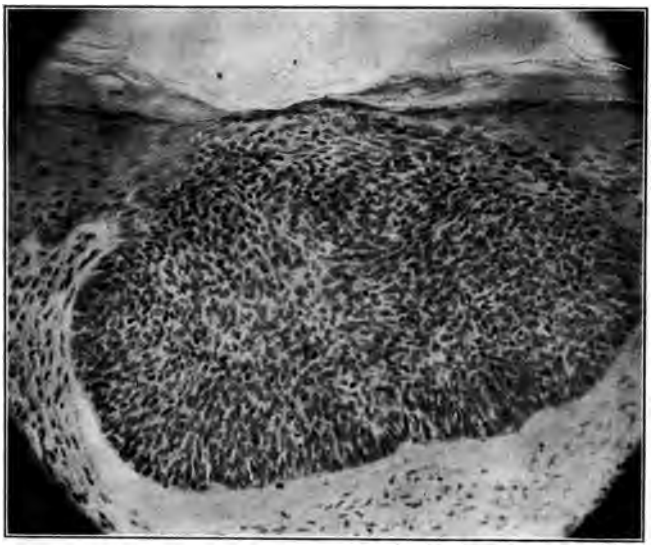

Fig. 15.—A later development of nodule in basal-celled cancer of skin shows ulceration of epithelium. (Gilchrist's case.)

selves in solid finger-like downgrowths (Fig. 17). The cystic degenerations are often very extensive, and it is not unusual to find numerous large cavities, surrounded by two or three layers of cancer cells. This stage is called *Carcinoma basocellulare* (*solidum et cysticum*). The growth may have a distinctly acinous arrangement, there being many fine branches, somewhat like the limbs of a tree. This condition forms the *Carcinoma basocellulare adenoides* of Krompecher, the *glandular epitheliomata* of the older writers, and the *tubular epitheliomata* of the modern dermatologists. In some of the large fungating neoplasms there may occur large or small stellate alveoli of cancer cells imbedded in granulation or fibrous tissue, so

as to somewhat resemble scirrhus carcinoma of the breast. Krompecher has no designation for this group, but Bloodgood calls them *Carcinoma basocellulare stellatum* (Fig. 18). In this latter group the cells may be so flattened out by pressure as to be almost unrecognizable, but they retain their affinity for the basic stains.

Clinical Course.—Clinically, these growths start upon a pre-existing dermatitis. Bloodgood states positively that in every case of which he has a complete history there was an antecedent lesion, however small. The commonest of these dermatoses is the so-called seb-

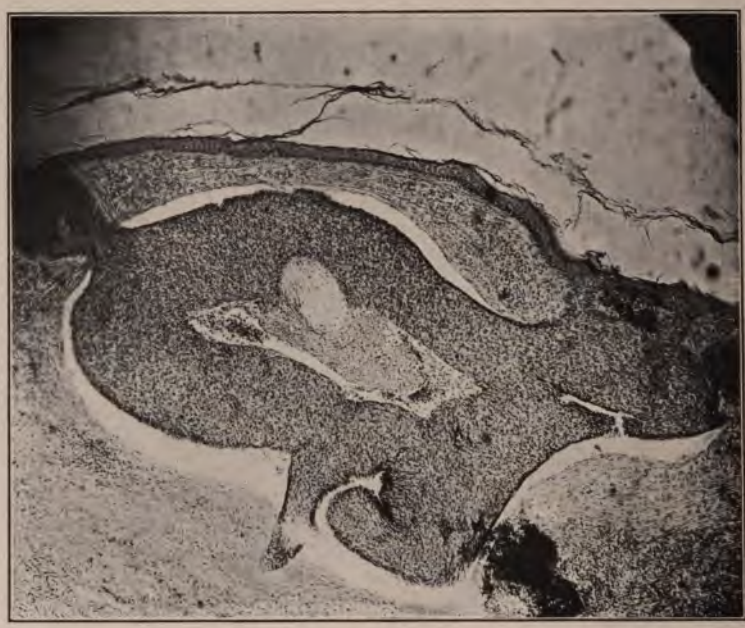

Fig. 16.—This section was from a typical rolled-edge rodent ulcer of the shoulders. The basal cells are arranged in solid masses. Notice the way that normal epithelium and some connective tissue cover the mass of cancer cells, while in other portions the growth may be seen springing from the surface epithelium. This invasive growth, without change in the overlying skin, is common in cancer and frequently leads to incomplete operations. (Author's collection.)

orrheic wart, next come small subepidermal nodules, then keratoses of various kinds, and finally scars or minute ulcerations, often thought to be traumatic. The first stage of the cancer that is noted by the patient is usually a slight itching or burning sensation, and at that time a very slight increase in thickness of the skin can be felt. Very shortly after a minute ulceration takes place and there is a serous discharge (Fig. 19). Then a scab forms, that drops off from time

Fig. 17.—This section also demonstrates the manner in which a basal-celled cancer may be covered by normal epithelium. This case had been treated by the x-ray and pronounced cured. Possibly too soft a tube was used.

Fig. 18.—In this low-power photomicrograph of a basal-celled carcinoma it can readily be seen that the cells are lying in small strands and also singly between connective tissue fibers. This histological picture is often seen in the large fungous basal-celled tumors, and at times makes them difficult to distinguish from spino-celled neoplasms. (Author's collection.)

to time, and whenever this occurs it is noted that the ulcerated area is a trifle larger. When examined closely, a few minute, greyish,

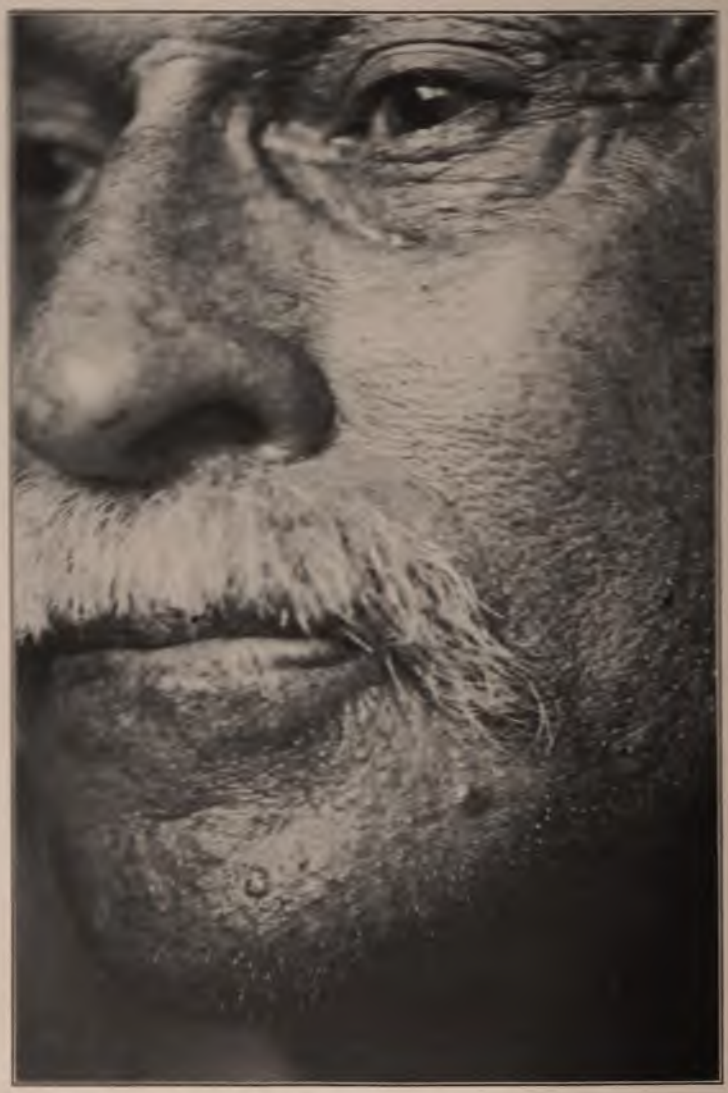

Fig. 19.—This man is suffering from two very early basal-celled cancers of his chin, proven by histological examination. They might be easily mistaken for benign growths at this stage, but slight crusting and oozing and a small amount of infiltration lead to their diagnosis. (Sutton's collection.)

shiny masses can be seen at the edge of the open sore, and this edge is usually hard and slightly elevated (Fig. 20). The neoplasm may

then take any one of several courses, all shortly to be described. When one of these growths is sectioned and examined in the gross, careful inspection will reveal a number of very fine whitish lines radiating downward from the tumor proper; these are the alveoli, filled with cancer cells. These white lines are very much finer than those occurring in the prickle-celled carcinomata, and should serve to differentiate between the two kinds at the time of operation.

All surgeons should become familiar with this class of tumors,

Fig. 20.—This young farmer is suffering from multiple basal-celled cancers. The oldest is of seven years' duration. (Sutton's collection.)

for they do not metastasize, and hence it is not necessary to remove the adjoining lymphatic glands. When glandular involvement is spoken of as occurring in this group of tumors, it is probable that

there is an error in diagnosis, and that the growth is really of cuboidal-cellular origin.

CLASSIFICATION OF BASAL-CELLED CARCINOMATA.

According to the later clinical course, the basal-celled carcinomata may be divided into seven groups—1, the flat rodent ulcers; 2, the nodular; 3, the rolled-edge; 4, the depressed scar-like cancer; 5, the morphea-like; 6, the fungating; 7, the deep ulcerating. All of these types may run more or less rapid courses, according to the rapidity of neoplastic growth, the nutrition of the part, and the resistance

Fig. 21.—This old lady has a flat basal-celled carcinoma of the nose, that has recurred after being curetted and cauterized with silver nitrate one year ago. The growth originally developed from a semi-globular wart similar to the one on the upper lip. (Author's collection.)

of the invaded tissue. If the cancer cells multiply more rapidly than they are able to invade, a fungous growth results. At times spontaneous healing may take place in the center, or even around the edges, but the whole growth never heals.

I. FLAT RODENT ULCERS.

Clinical Course.—The flat rodent ulcers usually occur upon the face (Fig. 21), and much more rarely upon the back. It is the most

frequent type encountered by the dermatologist and general practitioner. It begins as reddish or pearly-grey smooth nodule, 2 to 3 mm. in diameter. Superficial ulceration takes place early, owing to the invasion of the rete by the cancerous tissue. The ulcerated area is covered by a fairly closely adherent, black or dark-brown crust, which from time to time either drops off or is picked off by the patient. When this occurs, there is slight bleeding, and it is noticed that the ulceration is larger. The growth is always slow; it may take one year, or it may take five years, for a diameter of 1

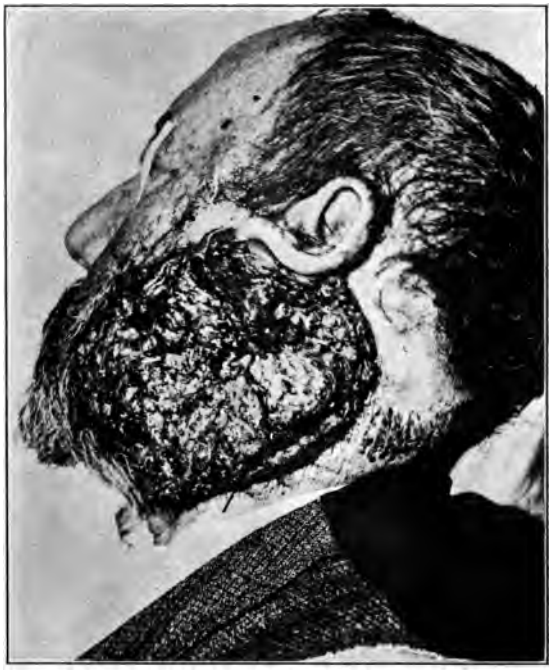

Fig. 22.—This basal-celled cancer is of many years' duration. Even more extensive ones occasionally come under observation. (Heidingsfeld's collection.)

cm. to be reached. Slightly enlarged blood vessels may be noted extending into the surrounding skin, and considerable induration is always present. On inspection, either with the naked eye or, if necessary, with a hand lens, a few pearly nodules can be seen just at the edge of the ulceration. The skin around the edge looks as though under great tension, is shiny and thin. The tissue beneath the scab resembles ordinary granulation tissue, but is less hemorrhagic and more friable.

Pathology.—If the growth be removed at this early stage and

examined histologically, it is at once seen that the new tissue consists entirely of basal cells, usually arranged in solid masses (*Carcinoma basocellulare solidum*). At times it will be noted that these solid alveoli are sending out finger-like downgrowths (*Carcinoma basocellulare adenoides*), or that distinct cysts have been formed (*Carcinoma basocellulare cysticum*).

Later Course.—If the tumor be undisturbed or ineffectually treated, one of several things may happen. In the first place, there may be widespread superficial ulceration, that may be so extensive as to cover half of the face (Fig. 22). In some of these cases it is remarkable how the mucous membranes are spared. Usually, however, the orbit is invaded, the eye destroyed, and death takes place

Fig. 23.—This basal-celled cancer has spontaneously healed in the center, but is spreading along the periphery. (Gilchrist's case.)

from meningitis. Second, the ulceration may take place as just described, but there may be some fungating masses, where the cancer cells are unable to rapidly invade the underlying tissue. Third, there may be considerable spontaneous healing, with the formation of a considerable central, white, depressed scar (Fig. 23). However, on at least one of the edges there is characteristic ulceration, or the formation of cancer nodules. In some of these cases the formation of scar tissue considerably distorts the features, pulling the eyelid downward, or the mouth upward as the case may be.

This, of course, is due to the contractures that always take place in scar formation. Fourth, the formation of deep cavities, due to severe ulceration may occur. Secondary infection frequently occurs, sometimes with pus producing organisms, and sometimes with putrefactive bacteria. The edge, even from a comparatively early stage is slightly elevated and always very hard, and at times cancer plugs may be distinguished in it, although this is much commoner in the prickle-celled cancers. The induration is due not only to the cancer cells, but also to the inflammatory cells, and to fibrous tissue that is frequently formed. The surface of the tumors is compara-

Fig. 24.—This portrays an early basal-celled carcinoma of the hand. Cancers upon the hand are usually spino-celled and metastasize. (Sutton's collection.)

tively smooth, resembling anæmic granulation tissue, and has not the rough, warty appearance, so characteristic of the squamous-celled tumors. The naked eye appearance of these neoplasma, upon section, is also characteristic; infiltration is usually comparatively shallow, and the white lines of invading epithelium are very fine.

Histologically, in the large growths, the early solid structure of the cancerous alveoli is never retained. The general arrangement is in more or less irregular cylinders, often branching, or in the stellate form described by Bloodgood. There is often much fibrous tis-

sue at the edges, and usually considerable inflammatory exudate, occasionally so severe as to obscure the cancerous picture.

Diagnosis.—In the early stages these growths may be confused with the nonmalignant keratotic conditions, or are rarely with simple inflammations. After ulceration has taken place only syphilis, lupus vulgaris, or more infrequently lupus erythematosis or even blastomycosis might simulate cancer. In the chapter on differential diagnosis there will be a full discussion of these diseases.

Fig. 25.—This nodular basal-celled carcinoma of the cheek arose from a seborrheic keratosis, a number of which may be seen upon the cheek. (Heidingsfeld's collection.)

II. NODULAR CANCERS.

Clinical Course.—The nodular cancers arise from a pre-existing lesion. A pearly nodule first forms, which slowly grows until in from six months' to one year's time the growth has attained a diameter of 1 cm. and an elevation above the skin of about the same. The lesion is roughly semiglobular in shape, may be slightly umbilicated, and is very hard and firm to the touch (Figs. 24, 25). The color is pinkish-white or grey, and there are dilated vessels ning into the tumor. Later, ulceration may take place in the ter (Figs. 26, 27), and the neoplasm run any of the courses al-

ready described under the heading of the flat rodent ulcer. This type is in reality simply a modification of the rolled-edge rodent ulcer type.

Pathology.—Histologically, the lesion at first shows the characteristics of the *Carcinoma basocellulare solidum*, but later changes to some of other types, as has already been described, the only difference being that the changes are comparatively slow, and that cysts rarely form.

Fig. 26.—This large basal-celled cancer of the hand sprang from a seborrheic keratosis. Notice a healed lesion upon the middle finger. This is an unusual tumor, for neoplasms of the hands are usually of the spino-celled type. (Sutton's collection.)

Diagnosis.—Gummata and benign epithelial, fibroid, or cystic tumors must not be mistaken for this type of growth.

III. ROLLED-EDGE RODENT ULCERS.

Clinical Course.—The rolled-edge rodent ulcer is very closely related to the two varieties just described, but more closely to the second type. It begins in the identical way that they do, but is fairly common upon the back and shoulders as well as upon the face. The tendency is for these tumors to grow much more rapidly than

the flat type, despite the fact that in many instances there is no surface ulceration for several years (Fig. 28). By the end of a year these tumors usually have a diameter of several centimeters. These growths have a distinctly semiglobular edge and a corresponding depression in the center, so that they resemble the crater of an extinct volcano. The edge is extremely hard, and the skin over it is tense, thin, and shiny, and there are numerous dilated blood vessels

Fig. 27.—This large basal-celled cancer, with a markedly elevated edge, arose from a seborrheic keratosis, numbers of which can be seen upon the face. (Heidingsfeld's collection.)

extending out into the normal skin. The skin of the central portion may or may not show signs of ulceration. If ulcerated, there is usually but a slight crust. The surface of the exposed or cancerous tissue resembles granulation tissue, and is anemic and friable. The late course of these neoplasms is the same as that of the two preceding types, and the pathology is identical with that of the nodular lesions.

IV. DEPRESSED SCAR-LIKE CANCER.

Clinical Course.—The depressed scar-like cancers are comparatively infrequent, the author's series containing but one case. As they start as a very small subepidermal nodule and as the skin over them remains intact, they frequently remain undiscovered for some little time. They usually arise upon the cheeks or temples of those well past middle life. The nodule flattens out, and slowly spreads along the basal layer of the rete, or just beneath it, and as a result the appearance is identical with that of a depressed scar, except that the color is not so white, and that the normal lines of the skin are to some extent retained. While the skin is thinner than usual, yet to examination it simply looks sunken and feels bound down, just as morphea patches do. There is no dilatation of the surface

Fig. 28.—This rolled-edge rodent ulcer of the neck has no ulceration, but is covered with a crust. (Heidingsfeld's collection.)

blood vessels. The induration can be plainly distinguished, feeling somewhat like a small coin imbedded beneath the skin.

These neoplasms grow very slowly, and ulceration does not take place until several years have elapsed. It is highly probable that tumors of this type may end in the morphea-like cancer shortly to be described.

Pathology.—The histopathology is the same as in the preceding group.

Diagnosis.—The differential diagnosis must be made from depressed scars, and from morphea.

V. MORPHEA-LIKE CANCER.

Clinical Course.—The morphea-like cancers have recently been described in detail by Heidingsfeld,[5] who has collected all of the reported cases in addition to describing one of his own. According

Fig. 29.—This morphea-like epithelioma showed upon histological examination typical basal-celled structure. (Heidingsfeld's collection.)

to Heidingsfeld, there are now but eight cases of this variety of cancer on record, but he calls attention to the fact that many cases of so-called ulcerating morphea should undoubtedly be put in this category. Cases have now been described by Danlos,[6] Stelwagon,[7]

[5] Heidingsfeld: Jour. Cutan. Dis., 1913, xxxi, 379.
[6] Danlos: Ann. de dermat. et de syphil., 1899, x, 656.
[7] Stelwagon: Trans. Amer. Dermat. Assn., 1899, 166.

Hartzell,[8] Fordyce,[9] Pernet,[10] and Heidingsfeld, and all of these authors feel that the cases are not especially rare, but that they are frequently overlooked. These lesions usually start as small nodules, situated upon the temples or malar eminences, but occasionally on the body. They are sharply defined and spread very slowly, it often taking four or five years for one to reach the diameter of 2 cm. When seen by the dermatologists, they are sharply-defined lesions, often with a slightly elevated pearly border. The center is white or yellowish-white, and is depressed. The violet hue, characteristic of scleroderma, is lacking, but there are dilated blood vessels running over the surface. The edge is very hard to the touch, and the center feels leathery (Fig. 29). There may or may not be small or fairly large ulcerated areas, either at the edge or nearer the center of the neoplasm. Pernet described the feel of the tumor as comparable to that of a coin imbedded in chamois beneath the skin, but other authors seem to think that it is not so hard as this. The tumors run the same course as any of the other slow-growing rodent ulcers.

Pathology.—Histologically, these neoplasms are usually of the acinous basal-celled type, undoubtedly starting as solid alveoli.

Diagnosis.—Morphea, or possibly syphilis or lupus erythematosis, might be confused with them.

VI. FUNGATING TUMORS.

Clinical Course.—Fungous tumors are either large or small. Occasionally a basal-celled neoplasm may be fungating from the beginning, but this is rare, and this characteristic is usually of late development. Fungation is caused by the cancer cells proliferating more rapidly than they can invade, so that the growth must necessarily be outward. The fungating surface may be covered with a slight scab, but frequently this is almost entirely lacking. The surface of the cancerous tissue is comparatively smooth, having but little of the rough, scraggly surface so characteristic of the prickle-celled tumors; in fact, it is even smoother than in cases of blastomycosis or papillary eczema. Again, the tissue resembles anemic granulation tissue, although slight trauma will cause free bleeding. In the smaller tumors the growth is very slow, and there is comparatively little induration beneath the surrounding skin. Sometimes a preexisting ulcer, either cancerous or otherwise, will sud-

[8] Hartzell: Jour. Amer. Med. Assn., 1909, liii, 262.
[9] Fordyce: Jour. Amer. Med. Assn., 1908, li, 398.
[10] Pernet: Ikonographia Dermat., 1912, vi, 243.

denly begin to fungate, a sure sign of renewed activity and rapid growth. And yet even in these cases metastatic growths do not occur. It is not unusual for the x-ray, radium, the ineffective use of caustics, or even of the curette combined with caustics to set up such a condition.

Pathology.—Histologically, these fungating tumors show either an acinous or a stellate arrangement of the cancer cells.

Diagnosis.—This class of neoplasms must be told from the rapidly growing fungating type of squamous-celled cancer, as well as from certain of the infections, as granulomata (granuloma pyogenicum, botryomycosis), recently so ably described by both Sutton[11] and Wile,[12] dermatitis vegetans, papillary eczema, blastomycosis, and simple exuberant granulation tissue.

VII. DEEP ULCERS.

Clinical Course.—Deep ulcers are rare, and in the majority of them it is probable that the growth consists primarily of cuboidal rather than of basal cells. They usually arise upon the face, grow rapidly, and, owing to a lack of resistance of the tissues, grow downward rather than upward; in other words, the fungoid growth is reversed. At the start they may have acted like typical rodent ulcers, but because of injudicious treatment, which injured the surrounding tissue, they may have found it much easier to penetrate deeply. The cancerous tissue has sloughed out, leaving a deep hole. The base of the ulcer is usually very ragged and dirty, there is frequently much discharge, often of a foul odor due to putrefactive bacteria, and the patient may be toxic from absorption. Death takes place from hemorrhage or from secondary infection, meningitis sometimes resulting.

Pathology.—Histologically, the cancer cells are usually arranged in long cylinders.

DIAGNOSIS.

In diagnosing basal-celled tumors from prickle-celled cancers, several factors must always be borne in mind. First, basal-celled tumors are common upon the face and fairly common upon the shoulders, but are very rare upon the limbs. Second, they usually originate from keratoses, and frequently from cutaneous abnormalities, frequently considered to be congenital. Third, their growth is usually

[11] Sutton: Amer. Jour. Med. Scien., 1911, cxlii, 69.
[12] Wile: Jour. Cutan. Dis., 1910, xxviii, 667.

comparatively slow. Fourth, their surface is rather smooth. Fifth, the induration is not as deep as in the squamous-celled neoplasms. Sixth, on section the infiltration is not so deep and the fine white lines of the cancerous alveoli are very fine. Seventh, on microscopical examination the cells are very different from the prickle cells, for they are smaller and stain more readily with the basic dyes, such as hematoxylin, while the prickle cells stain better with the acid dyes, such as eosin. The arrangement of cells is also different, there being no tendency for the basal cells to form whorls or pearls.

TREATMENT.

These tumors, even in moderately advanced cases, can be cured by sufficiently radical operation, for they do not metastasize except in very exceptional cases, and then only if there be a mixture of cuboidal cells. As regards treatment, there are several schools. The surgeons advocate the knife, and certainly show a very high percentage of permanent recoveries when the operation has been thorough. Certainly the actual cautery is even better than the knife, and it would seem to the author that when the knife is used the edges should always be treated with some caustic agent to prevent the multiplication of any cancer cells that might have been deposited upon the cut surfaces. Some believe that a combination of the curette and caustic is the best, and many adhere to the use of various cancer pastes or caustics. The x-ray has many advocates, and certainly some beautiful results have been secured with it. In the vast majority of instances the dermatologists have not attempted to check up their cases, Pusey[13] and Sherwell[14] forming two notable exceptions to this rule. Hence all cases reported as cured should not be taken too literally; the cases must be followed for at least three years before a cure can be pronounced. Bloodgood emphatically states that at least 50 percent of his cases that were cured by operation had been subjected to various caustics.

To the author's mind the rules of treatment are simple. If the production of a scar makes no difference the actual cautery should be used. This is simpler and better than excision followed by the use of a caustic, such as the acid nitrate of mercury, for the operator is not troubled by hemorrhage. If the growth is freely accessible and a small scar is allowable the knife may be employed, the edges swabbed with alcohol or a fairly strong antiseptic that will not produce deep necrosis, and the wound closed so as to produce a linear

[13] Pusey: Jour. Amer. Med. Assn., 1913, lxi, 552.
[14] Sherwell: Jour. Cutan. Dis., 1910, xxviii, 487.

scar. In small growths where they are not freely accessible, as in the naso-facial fold, or where it is important not to produce a scar, as upon the eyelid, the x-ray should be tried. It is important to give one or two heavy exposures of a measured dose, rather than to try many small doses, for recurrence follows many of the latter, and the growth is then resistant to further radiation. In absolutely inoperable growths either the x-ray or radium may be employed. However a small dose of radium should never be employed, or marked stimulation of the neoplasm may occur. In the case of extensive growth x-ray is the best method, for radium seems not to be applicable except in small tumors. In some instances a combination of these measures is to be advocated. For instance it is probably well to radiate after every operation. In all instances it is highly important not to employ measures that are insufficient, for such treatment is almost sure to result in the rapid spread of the cancerous process. Simple curetting, cauterization with silver nitrate, carbolic acid or similar substances, and the use of carbon dioxide snow should not be employed, as they usually do much more harm than good.

CHAPTER V.

CUBO-CELLED CARCINOMATA.

Origin.—It will be remembered that just above the cells forming the basal layer of the rete there is a layer of cuboidal cells, cells somewhat larger than the basal cells, and of a square rather than a columnar shape, and yet with no prickles and not staining as intensely with the acid dyes as do the prickle cells.

Epithelial tumors may arise from these cells, and when they do they possess characteristics of both the basal-celled and squamous-celled carcinomata, or, to be more exact, they form a connecting link between these two radically different types. They have many of the clinical characteristics of the former in that they grow rather slowly, and frequently run a course identical with that of the rodent ulcer, and yet they resemble the more malignant type in that they have a marked tendency to metastasize. At times it is practically impossible to distinguish them histologically from the basal-celled neoplasms, and Bloodgood[1] thinks that there are undoubtedly many mixed cases.

According to Bloodgood, these tumors were first recognized by Krompecher[2] in the course of his work on the histology of the basal-celled carcinomata.

Clinical Course.—Clinically, these growths arise from pre-existing lesions of the skin, just as do the other varieties of cancer. They may form either fungous or ulcerative lesions, but more usually the former. The tumors often grow very slowly; in a case reported by Bloodgood it took eight years for a diameter of 12 cm. to be reached. In the author's case (Fig. 30) a diameter of 10 cm. was reached in about six months; between these two extremes there are all stages of transition. The fungous neoplasms grow much more rapidly than the ulcers, and metastasis seems to take place sooner. The cancerous tissue resembles anemic granulation tissue, that bleeds easily and is very friable. There is always extreme induration about the edges.

Pathology.—The gross pathology is similar to that of the squamous-celled cancers, for the alveoli are large, much larger than in

[1] Bloodgood: Progressive Medicine, Dec., 1904.
[2] Krompecher: Der Basalzellenkrebs.

basal-celled growths, and contain fine white granular material (cancer cells) that can readily be squeezed out.

When examined under the microscope, it is seen that at first the growths are solid, but that they soon begin to spread out in long finger-like acini, that branch out more or less as they grow downward. The cells resemble large square basal cells, and at times are as large as the prickle cells, but do not contain prickles, nor do they stain with eosin as well as the spinous cells. In addition, there is no tendency for the formation of either whorls or the more advanced epithelial pearls.

Incidence.—Out of a total of 997 cases of epithelial tumors, of which 820 were malignant, Bloodgood[3] reports that there were 5

Fig. 30.—This cuboidal-celled cancer originated in a varicose ulcer of the leg, and had been present about five months. It has remained well for three years since local removal and cauterization. It would have been safer to have removed the glands. (Author's collection.)

percent of cuboidal-celled tumors. In location, these neoplasms are pretty well scattered. In a study of sixteen cases, Bloodgood states that three were on the lower lip, five on the face, three on the legs, and one each on the scalp, penis, tonsil, tongue, and neck.

Diagnosis.—The diagnosis must be made from both prickle- and basal-celled cancers, and in cases of a mixed type of tumor this may be very difficult. The naked eye diagnosis depends on the depth of the malignant infiltration, and the size of the alveoli, and the microscopic diagnosis on the size and character of the cells and the lack of whorls or pearls.

[3] Bloodgood: Amer. Jour. Med. Sc., 1914, cxlvii, 76.

Treatment.—If caught very early, simple excision with a wide margin will usually suffice to give a permanent cure, but, if the tumor has existed for any length of time, it is absolutely imperative to remove the neighboring lymph glands. Further study of this group of tumors is needed, as we are not yet clear as to when metastasis takes place, although late work by Bloodgood seems to show that this is often comparatively early.

CHAPTER VI.

SPINO-CELLED CARCINOMATA.

Occurrence.—In many ways this group of cancers forms the most important one from a clinical standpoint, for, when it is remembered that the lips, tongue, and penis are chiefly affected by this type, and that in addition a large proportion of the growths upon the cutaneous surfaces are prickle celled, it will readily be seen that the more important of the surgical epithelial cancers belong to this category. In a surgical service about two of these growths are seen to one basal-celled neoplasm, but in a dermatological service the reverse is the case. In the last forty cases of cancer of the skin seen by the author, nine were of this kind. According to the statistics of Bloodgood,[1] these tumors are most frequently encountered upon the lip; secondly, upon the skin; thirdly, upon the tongue; and, fourthly, upon the penis. In his review[2] of 60 cases from Bloodgood's service the writer found that the neoplasm upon the skin arose in the following localities: finger, 4 cases; hand, 11 cases; wrist, 2 cases; forearm, 2 cases; elbow, 2 cases; upper arm, 3 cases; foot, 2 cases; ankle, 3 cases; lower leg, 6 cases; knee, 2 cases; thigh, 3 cases; scalp, 3 cases; face, 8 cases; neck, 3 cases; trunk, 5 cases; and scrotum, 1 case.

Etiology.—For all practical purposes, the study of the precancerous lesions are the most important. In this same series of 60 cases the preexisting maladies were as follows: scar of burn, 11 cases; scar of trauma, 5 cases; sinus, 1 case; senile keratosis, 4 cases; "wart," 14 cases; "pimple," 5 cases; blastomycosis, 1 case; x-ray dermatosis, 2 cases; lupus vulgaris, 1 case; ulcer, 3 cases; scratch, 1 case; arsenic keratosis, 2 cases; uncertain, 10 cases. Upon the lips almost any variety of lesions may serve as the starting point, while upon the tongue lesions of leukoplakia or of syphilis are especially apt to become malignant.

Varieties.—Bloodgood formerly divided the spinocellular tumors into epithelioma spinocellulare and carcinoma spinocellulare, using the latter term when the typical arrangement of the benign prototype was lost. From a clinical standpoint there are but two types—

[1] Bloodgood: Progressive Medicine, Dec., 1904.
[2] Hazen: Jour. Cutan. Dis., 1915, xxxiii, 611.

the ordinary one of cancer and the other of the malignant wart that neither infiltrates nor metastasizes.

Clinical Course.—Clinically, the true cancers first appear as nodules that usually speedily ulcerate. They may then be either fungous or pure ulcers, or a combination of the two. The surface is usually rough and irregular, and is often papillary. The color is that of a dirty granulation tissue, with some whitish splotches. Around the edges there may be some cancer plugs, looking some-

Fig. 31.—Deep prickle-celled cancer of cheek in a young man. (Sutton's collection.)

what like comedones, from which masses of cancer cells can be squeezed. The tissue is friable and bleeds easily. The edge is usually very hard, and there is often deep induration. Growth is usually comparatively rapid, and it is not unusual to see extensive involvement by the end of the first year. A tumor of nearly 15 cm. diameter may be developed by the end of two months.

The most important thing to remember about this group of cancers is that they frequently metastasize. The author made a special study of this point in the paper already referred to, and has found that out of the 60 cases reported, 38 were followed for three years or

more, and that out of these 38 cases, 23 had definite metastases. In certain of these cases the metastatic growths apparently formed at a very early date, 4 when the primary growth was of not more than one month's duration. Spinocelled tumors of the body and head seem to be rather more apt to metastasize than those upon the limbs, and those originating from x-ray or arsenic keratoses seem especially dangerous in this respect.

The spinocelled malignant warts first appear as wart-like growths, which develop rather slowly. There is often a tendency toward pedunculation, and there is no cancerous infiltrate at the base. As a result, these growths do not form metastases.

Fig. 32.—Rapidly growing cancer developing from within the ear. (Heidingsfeld's collection.)

Pathology.—If one of these tumors be excised and then cut into halves, a number of interesting things may be seen by the naked eye—things that go a long way toward making an accurate diagnosis. There is usually rather wide and deep invasion of the corium; perhaps of the underlying muscle. Bloodgood states: "The epithelial alveoli are distinctly white in color, finely granular, and arranged in a more or less uniform papillary shape. . . . The fine, branching white lines are composed of masses of spinal-celled epithelium on a connective tissue basis." These lines are very much coarser than the lines in basal-celled growths, for in this latter condition the alveoli are usually comparatively small.

On histological examination a number of different types can readily be made out (Figs. 34, 35), although there is not as wide variation as in the histopathology of the basal-celled neoplasms. At the start the growth is usually solid; there is a dipping down of the rete, the new growth consisting almost entirely of prickle cells, but the basal membrane of cuboidal cells still remaining intact. Many of these prickle cells have lost their nuclei, in others atypical karyokinesis is going on; some of the cells have undergone various types of degeneration, already sufficiently discussed in chapter I, and there are considerable spaces between the cells. In addition to this,

Fig. 33.—Prickle-celled cancer originating in the mastoid following mastoid operation. (Heidingsfeld's collection.)

the prickles are disappearing. Other descending alveoli appear, not at more or less distant places, as so frequently occurs in the basal-celled growths, but as branches from the original downgrowth. The next appearance is where there are a number of solid alveoli, side by side, serial sections showing them to be connected and not separate and distinct. These solid alveoli may be large or they may be very small, so small as to be only four or five cells' diameter in thickness. In these early stages there is no tendency for whorl formation or the formation of epithelial pearls, but these changes may come very shortly, and are usually apparent about the time that the growth begins to divide into numerous small alveoli. These small

alveoli are, of course, the processes or buds that have been nipped off from the original parent growths. When one studies a comparatively late squamous-celled cancer of the skin, he will see that it usually conforms to one of four different arrangements: First, where a more or less papillary structure is maintained, all of the alveoli being about equal in size, and where the cuboidal basal cells are still found surrounding the prickle cells. In the center of these alveoli the cells are often found flattened out in a concentric shape, forming the well-known whorls, and distinct pearl formation may take place. Second, there may be very numerous small alveoli, each

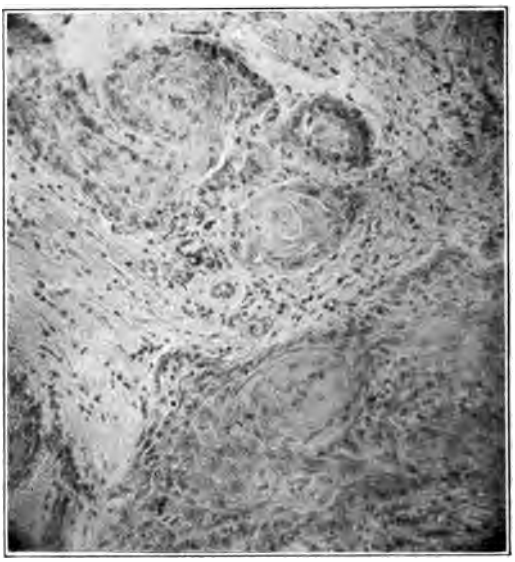

Fig. 34.—High-power photomicrograph of prickle-celled cancer. (Author's collection.)

composed of but a few cells, and separated from its fellows by connective tissue. In this form there are usually no basal cells discernible, and there is a great tendency for whorl or the more advanced pearl formation. Third, the neoplasm has a distinctly tubular formation, the cells being arranged in long lines that have many branches, which are rarely bordered by basal cells. And, lastly, the cell arrangement may be more or less that of a scirrhous carcinoma —that is, small islands of cells are found, surrounded by connective tissue. This type is analogous to the *Carcinoma basocellulare stellatum* of Bloodgood, except that here we have prickle instead of basal cells.

The cells themselves deserve study. They are large, more or less angular in outline, and stain intensely with the acid dyes, due to the presence of keratin. They retain none of their prickles, these being lost early in the course of the new growth. Especially have they undergone some of the types of hyaline degeneration already described. Where crowded closely together, the angular shape is lost and they appear as elongated spindle cells. Various types of atypical division can often be recognized.

There is usually considerable inflammatory exudate in the invaded tissue, an exudate that is greater than in most cases of basal-celled growths. This infiltration consists of small round cells, of fixed tissue cells, and occasionally of mast and plasma cells, an exudate that is comparable to that appearing in any chronic inflammatory dis-

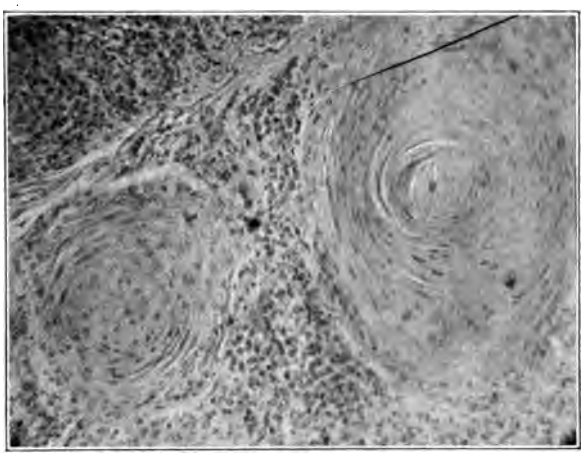

Fig. 35.—Epithelial pearls in a squamous-celled cancer. (Author's collection.)

ease; only rarely are there any great number of polymorphonuclear leucocytes, and then usually only when secondary infection has taken place.

As will be readily seen, the whole histological picture is essentially different from that found in the basal-celled growths; the cancerous alveoli are larger, invasion is deeper, there are epithelial whorls or pearls, the cells are much larger, and stain more intensely with eosin or orcein.

Prognosis.—Prognosis depends on the stage of the growth and the extent of the operation; even in fairly late cases the mortality should not be high if an extensive and thorough operation be done. The diagnosis must be made early if good results are to be obtained;

this is especially true in growths originating upon the lips, tongue, or penis, for here any delay usually results in extensive glandular metastasis.

Treatment.—In the opinion of the writer the treatment should be entirely surgical, leaving x-ray or radium for the so-called inoperable cases. It is true that Pusey[3] and others have obtained admirable results from the x-ray in many cases of this type of neoplasm, but the majority of other workers have not been so fortunate, presumably because they could not use their apparatus as efficiently as Pusey; hence it seems a form of treatment that is not suited for the majority of cases. Another objection is that it is difficult to determine when metastases to the neighboring glands have taken place, and, as Pusey himself admits, it is very unsafe to treat with the rays any tumor that has metastasized. Certainly no prickle-celled tumor arising from the mucous surfaces should ever be treated with the rays, unless the patient absolutely refuses operation, and, if such a treatment be attempted, the patient should sign a statement that he assumes all of the responsibility.

A complete excision of the tumor, of the underlying fat and fascia, of the lymphatic vessels and glands, all being removed in one piece, is the ideal operation. In a very early case, where the growth has existed but a week or two, complete local excision is sufficient if the growth be upon the skin, but not if it be upon mucous membrane. In small tumors a margin of at least half an inch should be given; in large tumors an inch or more, and the incision should always slope *away* from the tumor, so that a wide area of fat and underlying structure can be removed, and enough skin left for plastic work. In all of the late cases the neighboring glands should be removed, and it were better if the lymphatics connecting the site of the primary growth with the glands could be taken out in a block operation.

The problem in treating spino-celled cancers is to completely remove the local growth and also the draining glands. In a recent case under the care of Dr. H. H. Kerr and myself this problem was solved in an interesting way. The primary growth was situated over the junction of the parotid gland and Steno's duct, so that surgical removal would have necessitated dissecting out this gland and probably cutting the facial nerve. An attempt to dissect out the nerve in a cancerous field did not appeal as being good surgery. As a result Kerr did a block operation upon the glands of the neck, while the author subjected the primary lesion to deep radiation. The im-

[3] Pusey: Jour. Amer. Med. Assn., 1913, lxi, 552.

mediate results were excellent. Such a procedure probably has a rather wide field of usefulness.

The use of caustic pastes is mentioned only to be condemned; they do not reach sufficiently deep to destroy the outlying cells unless a great quantity is used, and then leave a wound that is a thousand times worse than any incision; in addition, they are very painful while being applied.

Articles concerning these neoplasms have been written by Borst,[4] Bloodgood,[5] Franz,[6] Borrmann,[7] Von Brunn,[8] Steiner,[9] McGlannan,[10] Volkmann,[11] and myself.[12]

[4] Borst: Die Lehre von den Geschwülsten, Wiesbaden, 1902.

[5] Bloodgood: Progressive Medicine, Dec., 1907, 1908, 1912; Jour. Amer. Med. Assn., 1906, xlvii, 1740; Amer. Jour. Med. Sc., 1914, cxlvii, 76.

[6] Franz: Beiträge z. klin. Chir., 1902, xxxv, 171.

[7] Borrmann: Deutsch. Zeitschr. f. Chir., 1906, lxxxii, 363.

[8] Von Brunn: Zentralbl. f. Chir., 1907, xxxiv, 550.

[9] Steiner: Deutsch. Zeitschr. f. Chir., 1906, lxxxii, 363.

[10] McGlannan: Maryland Med. Jour., July and August, 1908.

[11] Volkmann: Samml. klin. Vortr. Chir., 1889, No. 102.

[12] Hazen: Jour. Amer. Med. Assn., 1915, lxiv, 658; Southern Med. Jour., 1915, viii, 577.

CHAPTER VII.

BENIGN AND MALIGNANT TUMORS OF THE CUTANEOUS APPENDAGES.

As has already been pointed out, the normal skin has the following appendages: hair follicles, both of the lanugo and deep hairs, with the adjoining sebaceous glands, and the sweat glands and ducts. From all of these organs both benign and malignant tumors may arise. In addition, there is unquestionably the possibility of there being congenitally displaced epithelial or glandular tissue, and it now seems fairly certain that at least one clinical and pathological entity, the syringocystadenoma, springs from congenitally misplaced coil ducts. Dermoids, of course, have their origin in congenitally dislocated tissue.

Owing to the degenerative changes, as well as the modifications in cell type, that naturally take place during the lifetime of a neoplasm, it is highly probable that a fair number of tumors originate from these appendages, and that they cannot be diagnosed as such under the microscope. In even a slightly advanced basal-celled carcinoma, it is impossible to determine whether the origin was in the basal layer of the epithelium or in the hair follicle. As Unna[1] well points out, the cells of the sebaceous glands so readily revert to simple-appearing epithelial cells that one might never suspect a carcinoma of having its origin in them. From these two illustrations it can be readily seen that it is often impossible to say in just what cells the malignant change first appeared.

TUMORS OF THE HAIR FOLLICLES.

The hair follicle has different layers, just as has the skin, and epithelial growths may originate from any of these layers. Krompecher[2] states that he has been able to recognize two tumors of the face as springing from the basal layers of the hair follicles, and various other pathologists have reported similar observations. It is certain that, as our knowledge and technic improve, we shall later be able to identify neoplasms as springing from some of the numerous layers.

[1] Unna: Histopathology of Diseases of the Skin, New York, 1896.
[2] Krompecher: Der Basalzellenkrebs.

At the present time two different clinical and pathological varieties of tumor arising from the basal layer have been differentiated. The first is the *multiple benign cystic epithelioma,* subvariety of Von Zarisch, which is clinically indistinguishable from the more common type known as the Brooke-Fordyce[3] variety, where the growth is from the basal layers of the epithelium proper. These tumors will be fully discussed in the chapter dealing with the multiple benign tumors.

The second is the *rodent ulcer type,* or the *trichoepithelioma* of some authors.

The case reported by Bloodgood[4] is a fair illustration of this type. It occurred upon the cheek, just anterior to the angle of the jaw, in an elderly man, having been present for fourteen years as "a small elevated area covered with hair," probably a nevus of the hairy type. During the last year it had grown to about 7 or 8 cm. in diameter, and, as the result of the use of a caustic paste, there was a slight superficial ulceration, with considerable induration at the edge of the solid portion of the neoplasm. The tumor was freely movable over the cheek muscles. It was easily excised under cocaine, and it was then found that there was a zone of normal fat between the neoplasm and the underlying muscles. At the end of fourteen years there had been no recurrence. On section of the tumor the gross appearance showed large hair follicles, containing hairs in the depth of the tumor. Between the follicles the normal tissue was replaced by "a firm, white, granular tissue, divided into alveoli by a firm connective tissue stroma. Here and there were a few cavities, containing finely granular material—that is, the naked eye appearance of an epithelioma spinocellulare malignum." Histologically, however, the cells were not those of a prickle-celled carcinoma, but more nearly resembled basal or cuboidal cells, and in places could distinctly be seen springing from the hair follicles.

In Bloodgood's laboratory the author had the opportunity of studying another case in which the tumors were of much slower growth, and in which the cells were distinctly basal in character.

Recently the author has had a rather interesting case in his own practice. The patient was a man of 45, referred by Dr. Balloch, who had been struck upon the head two years previously, while on a fishing trip in the north woods. A few months later there developed a nodule, which had slowly increased in diameter. When seen, there was on the right anterior quadrant of the scalp a large growth that

[3] Sutton: Jour. Amer. Med. Assn., 1912, lviii, 333.
[4] Bloodgood: Prog. Med., Dec., 1904.

closely resembled a typical rolled-edge rodent ulcer. It was at least 12 cm. in diameter, the edge was very hard, and firmly attached to the skin, but not to the underlying bone. No ulceration had taken place. The hair was sparse, just as it was upon the remainder of his scalp. As operation would have been very difficult because of the size of the growth, it was determined to try the x-ray, and the results were very gratifying, for the growth promptly healed and for over two years there has been no recurrence. Histologically, the

Fig. 36.—Carcinoma originating in hair follicles. Low-power photomicrograph. (Author's collection.)

picture was very similar to Bloodgood's case (Fig. 36). There were very large hair follicles extending deep into the tissues; practically the whole field was filled with them, packed so closely together that there was no room for any other tissues. The hypertrophy was almost confined to the basal layers, and from some of them escaping strands of cells could readily be distinguished. The follicles contained no hairs.

In addition to the various types of cases mentioned above, it must

be borne in mind that some of the typical rodent ulcers, or basal-celled carcinomata, undoubtedly originate in the hair follicles.

TUMORS OF THE SEBACEOUS GLANDS.

At least four pathological types of tumors may arise from the sebaceous glands; first, simple hypertrophy, which clinically may give two different conditions—the well-known adenoma sebaceum and, in addition to this, irregular nodulations, often known as rhinophyma; second, true adenoma of the glands, which condition may also be found in adenoma sebaceum according to Sutton;[5] third, a basal-celled carcinoma; and, fourth, an adenocarcinoma arising from the inner and more differentiated layer of lining cells.

Adenoma Sebaceum.—The subject of adenoma sebaceum will be fully discussed in the following chapter. Simple hypertrophy of the sebaceous glands also appears at times as an accompaniment of other diseases, and at times as independent tumors. The independent tumors are rare; they are isolated, grow slowly, are yellowish-white in color, opaque, and usually from 3 to 6 cm. in diameter, semiglobular in appearance, but globular to the palpating finger, and often show a gaping follicle. At times sebaceous material can be squeezed from them. Much more frequent are the hypertrophies associated with rosacea and histologically combined with proliferation of the fibrous tissue. This condition usually occurs upon the nose, but may to a slighter extent involve the cheeks and forehead.

True Adenoma of the Glands.—True adenoma of the glands are practically unknown according to Unna, but Sutton thinks that in one of his cases of adenoma sebaceum he is justified in considering that this condition was present.

Basal-Celled Carcinoma.—As Krompecher points out, the basal cells of the skin form an unbroken line with the basal cells not only of the hair follicles, but with those of the sebaceous glands as well, so that *a priori* there is reason to believe that basal-celled tumors may originate from them; he offers no proof, however, that such neoplasms do exist. Thiersch thought that very many of the cylindroma (epithelioma basocellulare adenoides) had their origin in the sebaceous glands, but his deductions were founded entirely upon the fact that the arrangement of the cells in this condition resembled the arrangement of the cells in the sebaceous glands, and that the lobular shape of the two was somewhat alike; hence his views were speedily overthrown. It must be remembered that a tumor could

[5] Sutton: Jour. Cutan. Dis., 1911, xxix, 480.

easily originate from these cells, and that after a slight period of time it would be impossible to prove or even suspect this fact. While this fact is by no means proven, yet the author feels convinced that such must be the case.

Adenocarcinoma.—Unna states that one of his seventy-three cases arose from the sebaceous glands, and still retained the characteristics of the sebaceous-cell type. He calls particular attention to the fact that in any inflammatory or neoplastic condition the cells lose their fat, and revert to a simple cuboidal epithelial type, impossible to differentiate from other epithelial cells. Bloodgood mentions none of his tumors as of this class. Nor is any of the recent literature helpful on this class of tumors. Recently the author has seen a remarkable case of adenocarcinoma of the sebaceous glands where the cell type was completely retained (Fig. 37). The patient was a middle-aged negress, admitted to the surgical service of the Freedmen's Hospital because of a fungating tumor that had existed upon her left buttock for one year. She stated that it had started as a nodule beneath the skin, which had rapidly grown and speedily ulcerated. On examination a large part of the buttock was involved by a deeply-seated tumor that had ulcerated through the skin and become markedly fungous. In the nearby skin were several similar smaller neoplasms. The left inguinal glands were markedly enlarged. On biopsy it was found that the tumor consisted entirely of enormously enlarged and dilated sebaceous glands, more or less filled with an albuminous material. The lining cells were but one or two rows thick, and had retained all of the characteristics of sebaceous gland cells. A few of the cells had, however, escaped through the basement membrane. There were numerous mitotic figures. All of the cells contained fat, and were of the same size and general characteristics as normal gland cells. Unfortunately the patient refused operation and was lost sight of.

TUMORS OF THE SWEAT GLANDS.

Here, again, there are several possibilities: First, simple hypertrophy of the sweat glands; second, true adenoma of the sweat glands; third, basal-celled carcinoma of the sweat glands; and fourth, more malignant carcinoma, springing from the lining cells of the sweat glands.

Simple Hypertrophy of the Sweat Glands.—Simple hypertrophy of the sweat glands does not form tumors, so far as is now recognized.

True Adenoma of Sweat Glands.—Unna states that definite adenomata of the coil glands are very rare, and that most tumors usually supposed to consist of these elements are in reality derived from the sweat ducts. As a criterion, it is necessary to show that lateral growths spring from the glands, these growths tending to

Fig. 37.—This carcinoma of the buttock arose about one year ago, and is now practically inoperable, owing to a mass of glands in the groin. Histological examination showed that the neoplasm still retained the structure of the sebaceous glands, from which it arose. This proves that an adenocarcinoma of the skin may metastasize rapidly, and that the glands should be taken out at the earliest possible moment. (Author's collection.)

bend and roll up; the presence or absence of a lumen is of no particular moment, but the basal membrane must be intact. The true cases of spiradenoma fall into two groups, according to whether they form true independent tumors, or are simply accompaniments of other dermatoses. The former are rare, the latter fairly common. The latter type is most frequently encountered in association with carcinomata and angiomata, also in lupus and neurofibromata, as well as varices of the leg.

Unna has collected six cases which he accepts as true spiradenomata—the cases reported by Lotzbeck, Thierfelder, Knauss, Chandelux, the Haggans, and one of his own. Most of these tumors arose as subcutaneous nodules, which grew either slowly or rapidly, but which were always encapsulated. Usually there was considerable accompanying vascular dilatation. Unna's review of these cases is very complete.

Adenocarcinoma of Sweat Glands.—Carcinomata of the sweat glands are comparatively rare tumors, and must usually be derived from the basal cells, for they are of comparatively slow growth. They arise as nodules beneath the skin, which gradually become adherent to the surrounding tissues and eventually ulcerate. Bloodgood has seen but two cases. His second case is described as follows:[6] "It was observed in a colored woman aged 50 years. Two years ago attention was called to the back by itching; the patient felt a small nodule in the back, about the size of a bean, since which time there has been a steady growth, and the patient has abraded the surface by constant scratching. . . . The central ulceration is very superficial, like an abrasion, and covered with a brownish crust. This ulceration occupied the center of an oval, with a slightly elevated area of induration not sharply outlined from the surrounding tissue. Clinically, it appeared like a diffuse fibroma of the skin, which is not an uncommon observation, especially in the colored race. . . . On section between the superficial ulcerated area and the surrounding zone of epidermis, one could see nothing but a diffuse growth of fibrous tissue. Epithelial alveoli could not be distinguished with the naked eye; yet, when studied microscopically, this fibrous stroma was riddled with minute areas lined or filled by sweat gland epithelium, and in many places the long tubules of the sweat glands were preserved." With all due deference to the great authority of Bloodgood, the author feels that this tumor is an example of an adenoma of the sweat ducts, rather than

[6] Bloodgood: Prog. Med., Dec., 1904.

a carcinoma of the glands. In a recent article Wolfheim[7] states that there are but two certain cases of this disease on record—a case of Darier's and one of his own. Wolfheim contends that the following criteria are necessary in order to establish beyond all doubt this diagnosis: first, either a sure connection with the ducts or coil glands; second, a morphology which can be identified without any doubt as normal or abnormal sweat glands; and third, the condition of the elastic tissue must be investigated, because its characteristic arrangement around the tumor mass indicates whether we have to do with sweat gland tissue. Klauber[8] has given an excellent review of the subject.

Fig. 38.—Low-power photomicrograph of adenoma of the sweat ducts. (Author's collection.)

TUMORS OF THE SWEAT DUCTS.

Here also there are several possibilities—first, benign tumors of the ducts, and, second, carcinomata arising from the ducts. Also, it must be remembered that the multiple syringocystadenomata spring from congenitally displaced sweat ducts.

Benign Tumors of the Ducts.—The benign tumors, or syringoadenomata, are usually solitary, or occasionally multiple tumors, and

[7] Wolfheim: Arch. f. Dermat. u. Syphil., 1907, lxxxv, 277.
[8] Klauber: Beitr. z. klin. Chir., 1904, xli, 311.

are apt to appear upon the face as semiglobular nodules, which on palpation are easily distinguished as globular, but which are not adherent to surrounding tissue. They vary in diameter from 1 to 8 cm. Histologically, they consist of many lateral branches from the ducts, the lumens of which may or may not be patent, but the basal membrane of which is never broken through. Besides the increase of epithelial tissue, there is an increase of fibrous tissue as well (Figs. 38, 39).

Petersen has described a case of clinical "nevus unius lateralis" which consisted chiefly of a true syringoadenoma, and Unna has had

Fig. 39.—Adenoma of sweat ducts. High-power photomicrograph. (Author's collection.)

a somewhat similar case, and which he described as "asphyxia reticularis multiplex."

Carcinomata of the Ducts.—Carcinomata of the ducts have not been described, but doubtless occur.

Treatment.—The treatment of all of these tumors is fairly definite. When a tumor is clinically benign, it may be treated by simple excision, and, when clinically malignant, by broad local removal, usually without disturbing the lymph glands. If, however, microscopical examination shows a malignant type of carcinoma, the glands should be removed at once. If good frozen sections can be obtained

at once, this further operation may be done at the same sitting, as otherwise a second operation is necessary. In inoperable cases one might resort to radium, the x-ray, or the curette and cautery. Irritant pastes should never be used, for the growth is usually too deeply situated to allow of curative results.

CHAPTER VIII.

MULTIPLE BENIGN TUMORS.

The three varieties of multiple benign tumors of epithelial origin —namely, the multiple benign cystic epithelioma, the syringocystadenoma, and adenoma sebaceum—have recently been thoroughly studied by Sutton,[1] and the following account is largely derived from his articles.

MULTIPLE BENIGN CYSTIC EPITHELIOMA.

These tumors were first studied histologically by Balzer and Menetrier[2] in 1885, but they failed to recognize the true nature of the growths. Brooke[3] in 1892 and Fordyce[4] in the same year independently investigated the lesions and arrived at a proper solution of the problem.

Clinical Course.—Clinically, the disease is more apt to occur in women (Fig. 40), usually those past middle life, and there is a marked tendency for the disease to run in families, several members frequently being involved. The site of predilection is the face. The tumors are translucent and vary in size from 2 to 8 mm. in diameter. They vary in number from six to twenty. Usually the growths remain stationary for many years, a few new ones occasionally appearing, but the older ones showing no tendency to either enlargement or to spontaneous disappearance. In a few cases malignant change has taken place, this having occurred in the cases reported by J. C. White,[5] Jarisch,[6] Stelwagon,[7] Sutton and Dennie,[8] and Strobel.[9] Heidingsfeld[10] is inclined to believe that all tumors of this class are premalignant in both structure and character, but Sutton strongly dissents from this view.

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[1] Sutton: Jour. Amer. Med. Assn., 1912, lviii, 333.
Jour. Cutan. Dis., 1911, xxix, 480.
Amer. Jour. Med. Sc., 1913, cxlv, 819.
[2] Balzer and Menetrier: Arch. f. Physiol., 1885, 565.
[3] Brooke: Brit. Jour. Dermat., 1892, iv, 269.
[4] Fordyce: Jour. Cutan. Dis., 1892, x, 459.
[5] White: Jour. Cutan. Dis., 1894, xii, 477.
[6] Jarisch: Arch. f. Dermat. u. Syphil., 1892, 269.
[7] Stelwagon: Diseases of the Skin, Phila., 1910.
[8] Sutton and Dennie: Jour. Amer. Med. Assn., 1912, lviii, 333.
[9] Strobel: Personal communication.
[10] Heidingsfeld: Jour. Amer. Med. Assn., 1912, lvix, 256.

Pathology.—Histologically, there are two distinct types—the Brooke type, where the tumor is derived from the basal layers of the rete, and the Jarisch type, where the proliferation is from the hair follicles. In both types the picture is somewhat similar, for "extending down into the corium from the basal layer were numerous fine, long, slender chains of epithelium, two or three cells in width, which terminated in bulb-like cysts, filled with colloid material and corneous material." These collections of horny matter are undoubtedly snared off from the horny layer, as so well illustrated by Krompecher in examples of the basal-celled tumors. In

Fig. 40.—Multiple benign cystic epithelioma. (C. J. White's collection.)

some cases there is an additional subdividing of the downgrowths. In addition to these changes, cysts are found in the upper portion of the prickle layer, filled with hornified material. There may be a considerable amount of small round infiltration in the corium (Fig. 41).

Nomenclature.—Inasmuch as the cells are distinctly basal in character, the author feels that the name proposed by Unna[11] and adopted by Sutton—namely, *Acanthoma adenoides cysticum*—is an unfortunate one, for the term acanthoma should refer entirely to tumors

[11] Unna: Histopathology of Diseases of the Skin.

derived from the prickle layer. The name *Basocelluloma adenoides cysticum* would be nearer the correct term, and only the disinclination to further incumber the dermatological nomenclature prevents the author from adopting it.

SYRINGOCYSTADENOMA.

This group has likewise been well studied by Sutton, and his finding confirmed by Welch. For this group of tumors there have been many names proposed, largely because of the uncertainty as to the

Fig. 41.—Low-power photomicrograph of multiple benign cystic epithelioma. (Sutton's collection.)

true pathological picture. It has been repeatedly confused with the group just described. Biesiadecki[12] and Kaposi[13] called these growths "Lymphangioma tuberosum multiplex;" Quinquad,[14] "Cellulome epitheliale eruptif;" Besnier,[15] "Nevi epitheleaux cystiques;" Waldheim,[16] "Hemangioendothelioma cutis papulosum;" and Gassmann,[17]

[12] Biesiadecki: Untersuchungen aus dem path. u. anat. Inst. im Krakau, 1872, 2.
[13] Kaposi: Hebra's Lehrbuch der Hautkrankheiten, Enke.
[14] Quinquad: Trans. Internat. Congr. Dermat., Paris, 1889, 412.
[15] Besnier: Besnier and Doyen's Translation of Kaposi Pathol. u. Therapie der Hautkrankheiten, ii, 367.
[16] Waldheim: Arch. f. Dermat. u. Syphil., 1902, 225.
[17] Gassmann: Arch. f. Dermat. u. Syphil., 1901, lviii, 177.

"Nevi cyst-epitheliomatosi papulosum." In addition to these names, many others have been given from time to time.

Clinical Course.—Clinically, these tumors appear as numerous translucent semiglobular growths (Fig. 42), varying in diameter from 2 to 8 mm., and usually situated on either the chest or face. Women appear to be more subject to them than do men. They persist in-

Fig. 42.—Syringocystadenoma. (Sutton's collection.)

definitely, neither growing in size, nor tending to disappear. They do not undergo malignant change.

Pathology.—Pathologically, the stratum corneum is unchanged (Figs. 43, 44), the granular layer is somewhat thinner than normal and is devoid of granules, and the basal layer is regularly arranged, but the cells are swollen and edematous, and the nuclei large and vesicular. The papillæ are flattened, or perhaps lacking. There is some cellular infiltration in the upper portion of the corium, but the blood vessels are lessened in number and show no inflammatory changes, the capillary endothelium being normal. The elastic tissue is reduced in amount, and an elastic membrane completely sur-

rounds the cysts. Hair follicles and sebaceous glands appear to be normal. The coil glands are well developed and exhibit no pathological changes. There is some collagenous degeneration of the connective tissue stroma. Scattered throughout the cutis, from the subpapillary portion of the corium to the subcutaneous fat, are numbers of round or oval masses of epithelium and epithelial lined

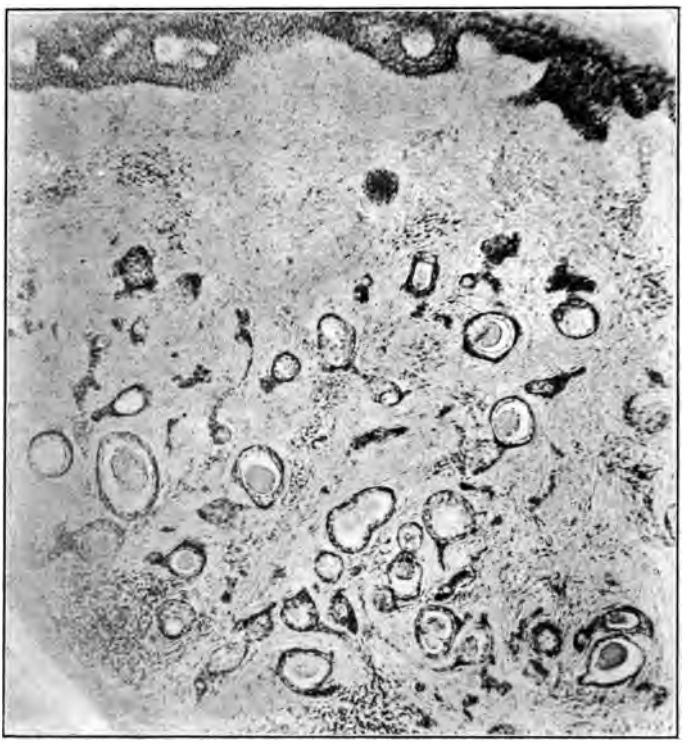

Fig. 43.—Low-power photomicrograph of syringocystadenoma. (Sutton's collection.)

tubules. Many of these cell collections possess a stem-like appendage of epithelial cells, two cells in thickness, which connect two or more of the gland-like masses. In many instances these epithelial tracts are found existing through the corium. The nuclei of the cells is large and stains deeply. In macroscopically normal skin taken from the trunk Sutton has found similar strands of epithelial cells, and in one specimen several budding processes and a few cysts were present. That these cells still retain their function was proven by Sutton by administering pilocarpine to the patient, sweat appearing upon the surface of the tumors.

Origin.—There is still a question as to whether these tumors spring from previously normal sweat ducts, or from congenital or acquired defects. Török[18] holds that the absence or rare occurrence of sweat glands in the area of the tumor, compared to the number in the adjoining normal skin, is indicative of the transformation of the preexisting sweat tubules into tumor elements. In favor of the congenital theory is the occurrence in so many instances of the tumor in early life, and especially in several members of the same family. Schidachi[19] has produced similar cysts, even with epithelial strands, by occluding the sweat ducts. Stockmann[20] has shown that the sweat tubules contain genuine secretion, and in one of Sutton's cases there was an enlargement of the tumor following the use of

Fig. 44.—Low-power photomicrograph of syringocystadenoma. (Strobel's case.)

pilocarpine. Sutton strongly contends that the growths are derived from congenitally misplaced sweat ducts.

ADENOMA SEBACEUM.

According to Sutton, Rayer[21] was the first to describe adenoma sebaceum, calling it "Vegetations vasculaires." A few years later

[18] Török: Monatshefte f. prakt. Dermat., 1892, xiv, 185.
[19] Schidachi: Arch. f. Dermat. u. Syphil., 1907, lxxxiii, 3.
[20] Stockmann: Arch. f. Dermat. u. Syphil., 1908, xlii, 145.
[21] Rayer: Rayer's Treatise, 2d ed., Willis's Translation, 996.

Addison and Gull[22] considered it to be a lichen. In 1890 Pringle[23] accurately described the histology of the lesions, and typical cases are often called the "Pringle type" of adenoma sebaceum.

Clinical Course.—The lesions are not often seen in private practice, and are only exceptionally encountered in the dispensary, but Crocker[24] states that in insane asylums plenty of them can be observed. The lesions are discrete, red nodules, varying in size from 1 to 9 mm., and situated upon sides of the nose and the adjacent portions of the cheeks (Fig. 45). They may, however, be scattered

Fig. 45.—Adenoma sebaceum. (Author's collection.)

upon any other portion of the face. The surface capillaries are dilated, thus giving the bright red color. The lesions tend to run in families, just as the above described conditions do. A low grade of mental development not infrequently accompanies the cutaneous condition. Poor considers that there is another type of adenoma sebaceum, in which the eruption is asymmetrical, and the lesions tend to coalesce. Krzystalowicz considers that there are two pathological varieties—one a true hypertrophy of the sebaceous glands, which

[22] Addison and Gull: Guy's Hospital Reports, ser. 2, vii, 267.
[23] Pringle: Brit. Jour. Dermat., 1890, xii, 1.
[24] Crocker: Diseases of the Skin.

may undergo degeneration, and a second which seems to include pathological deviations.

Pathology.—In a recent case of Sutton's, two tumors were excised, and his report is appended in a somewhat abbreviated form. The smaller growth was made up of two imperfectly formed and empty hair follicles, with subjoined masses of enormously hypertrophied sebaceous glands, the larger of which connected directly with the surface. The cells and nuclei stained clearly and well. Two of the larger masses of glandular tissue were divided into separate lobules by fine, fibrous septa. The larger tumor more nearly

Fig. 46.—Molluscum contagiosum. (Author's collection.)

fulfilled Unna's requirements for a true steatadenoma (a benign tumor-like growth of irregular formation, proceeding from the epithelium of the sebaceous glands, in the outgrowth of which fatty, but no colloid metamorphosis, takes place). Surrounding the lower third of an abortive hair follicle were numerous small, oval, or irregularly oval collections of sebaceous glands. No horny pearls or colloid substance was found. The individual cells in the sebaceous masses were smaller and less plump than those observed in the growth described above, and the number of the lobules was increased threefold. To sum up, in one growth there was a hypertrophy of

the sebaceous tissue, and in the other the formation of new glands.

In one case that the author has personally studied the sebaceous glands were but very slightly hypertrophied, the blood vessels were dilated, and there was considerable perivascular infiltration in the upper portion of the corium.

Atypical Multiple Growths.—The above descriptions are characteristic of the typical growths, but various authors have described various atypical multiple growths of a benign nature, and clearly of an epithelial origin. Hartzell[25] has reported a unique neoplasm which resembled both the multiple benign cystic epithelioma and the syringocystadenoma, and which may have been a combination of the two. Ormsby[26] has reported a case of comparatively large tumors in which spontaneous involution took place, and which clearly sprang from the sweat ducts, which were filled with and surrounded by thick masses of epithelial cells.

Diagnosis.—There are comparatively few conditions which simulate these multiple benign epithelial growths. One condition that must be excluded is molluscum contagiosum (Fig. 46) and another colloid milium. The former of these comes on suddenly, and often occurs in epidemics. There is a marked central depression, and, on opening, gelatinous material can be squeezed out. Colloid milium usually develops upon the upper part of the face, there is no dilatation of the surface capillaries, and the lesions are distinctly yellowish in color.

Prognosis.—The prognosis is good so far as life is concerned, but the lesions persist indefinitely.

Treatment.—All of these tumors can be removed by the knife, curette, caustics, electrolysis, and at times by the x-ray. Personally, the author prefers the electric needle.

[25] Hartzell: Brit. Jour. Dermat., 1904, xvi, 361.
[26] Ormsby: Jour. Cutan. Dis., 1910, xxviii, 433.

CHAPTER IX.

NEVOCARCINOMATA AND MALIGNANT MELANOMATA (MALIGNANT PIGMENTED MOLES).

It is a rather curious fact that, although it has been known for many years that the most malignant of all tumors spring from the skin and are deeply pigmented, yet only within the last ten years has the significance of that fact been generally recognized. In 1903 Keen[1] and Bloodgood,[2] independently, showed that these growths almost always, if not invariably, spring from moles or nevi, and recommended that such growths be removed as a prophylactic measure.

In dealing with the clinical forms, it is wise to bear in mind the words of Unna,[3] who states: "Since the melanocarcinomata of the skin always take their origin in pigmented moles, and, on the other hand, there can hardly be nevocarcinomata completely without pigment, it is well to describe together these two groups of tumors, which are combined by gradual transitions. And, further, in every other aspect, the character of the two is the same. In all cases we are dealing with rapidly growing, pigmented carcinomata, of alveolar structure, which soon lead to infection of the lymphatic glands, to more or less melanotic metastasis and a fatal termination."

Clinical Course.—Clinically, these tumors have their origin in nevi, using the term in its broad sense, most frequently from either congenital or acquired, almost flat, deeply pigmented moles of the nonhairy variety. It is usually noted that a mole, usually one that has been subjected to trauma, begins either to grow or to ulcerate, these changes usually not being especially marked. Metastases frequently develop before any change has been noted. The general impression among the profession seems to be that these metastases usually involve the skin and the viscera, and that the lymph glands are spared, but this view is by no means the correct one, for in the vast majority of instances there is marked glandular involvement. Clinically there are four main courses, which, of course, grade off, one onto the other. First, it may be noted that, very soon after changes are noted in the mole (or nevus), numerous other pigmented spots make their appearance in the skin, looking very much like other

[1] Keen: Jour. Amer. Med. Assn., 1903.
[2] Bloodgood: Progressive Medicine, Dec., 1903.
[3] Unna: Histopathology of Diseases of the Skin.

Fig. 47.—This figure shows widespread cutaneous metastases from a malignant pigmented mole (nevocarcinoma). There were also visceral growths. (J. W. Perkin's collection.)

moles (Figs. 47, 48). They usually, however, grow rather rapidly; some of the glands begin to enlarge; a number of fairly large, more or less pigmented, tumors appear on or in the cutis, and signs of

visceral disturbance arise, from which the patient speedily dies. Second, there may be marked evidence of metastasis in some of the internal organs, usually the liver, and but few cutaneous symptoms; there may or may not be glandular enlargement. Third, there may be very marked involvement of the neighboring glands, without any other signs of trouble than the changes in the mole. As a general rule in this type, the tumor growth at the site of the mole is comparatively large. These cases may live for a number of years.

Fig. 48.—Two years ago this patient had an ordinary pigmented mole on his back that was irritated by his suspenders. It has now become malignant, and has recurred in spite of an extensive operation. There are also malignant growths in the skin and viscera. (Heidingsfeld's collection.)

Fourth, involvement of the glands does not become apparent for a number of years, and further extension is but slow. The first three forms do not require to be proven by illustrations, but the last type is sufficiently rare to merit a case report. The patient was a woman aged 50, who entered the Johns Hopkins Hospital, with the following history. She was a farmer's wife from Maryland, and had an

ordinary deeply pigmented mole upon her forearm, that was one day pecked by a hen so as to bleed. Several months later the mole began to grow, and slight ulceration began to manifest itself. The growth was excised by a local physician. Almost a year later local recurrence took place, and this was again excised. Two years later there was another recurrence, and there was wide operative removal; at the same time a number of enlarged, deeply pigmented glands were taken out from the lower portion of the axilla. Two years later, or five years from the appearance of the original trouble, there was an inoperable recurrence in the axilla. In this case early amputation, or possibly a complete removal of the axillary glands, would have saved the life of the patient.

These growths are especially liable to show themselves in certain localities. They may appear upon the face, arms, or body, but also upon the sole of the foot, especially in women, and at times under the finger nail, forming the so-called melanotic whitlows.

Pathology.—Pathologically, they always spring from nevoid cells, and it is still a matter of dispute as to whether these cells are of epidermal or of mesoblastic origin; hence it is questionable whether the tumors should be called carcinomata or sarcomata. Fordyce[4] has recently reviewed the question very thoroughly, and the following account is largely derived from his excellent article. Following the work of von Demieville[5] in 1880 and von Recklinghausen[6] in 1882, these neoplasms were regarded as endothelial in origin until 1893, when Unna promulgated his now well-known views that they were of epiblastic descent. Unna states: "From the fact noted in describing nevi, that the well-known cellular cords of soft nevi consist of true epidermic epithelium, which has been snared off from the surface epithelium in the embryonic period or in early youth, the development of cancer in them is quite comprehensible, indeed self-evident." Krompecher,[7] too, agrees with Unna, stating that the masses of nevoid cells can be seen springing from the basal layer of the epidermis in many instances; that, furthermore, they can be demonstrated to arise directly from the basal cells. He states definitely that the prickle cells do not degenerate into nevoid cells, as Hodara[8] says. Gilchrist has shown the same things as Krompecher.

On the other hand, many pathologists hold that the nevoid cells,

[4] Fordyce: Jour. Amer. Med. Assn., 1910, liv, 91.
[5] von Denieville: Virchow's Arch. f. Path. Anat., 1880, lxxxi, 333.
[6] von Recklinghausen: Über die Multiplen Fibrome der Haut, Berlin, 1882.
[7] Krompecher: Der Basalzellenkrebs.
[8] Hodara: Monatsh. f. prakt. Dermat., 1897, xxv, 205.

especially the chromatophores, have their origin in the mesoderm. On this side are grouped Virchow, Soldan,[9] Borst,[10] Kreibich, Ribbert,[11] and Adami.[12]

Johnston,[13] in a very complete article, decides that nevi are usually of endothelial origin, springing from the lymph vessels. Fordyce holds that nevi may have a twofold origin. He states: "In some the character of the cells conforms more closely with those of the epidermis, and can hardly be distinguished from the prolongations of the latter, which enter the mole. In others there appears to be another variety, consisting of cells with vesicular nuclei, with faint or no tinctorial properties and a well-defined border. Their shape in general is round, but this may be modified by mutual pressure. Fibers from the connective tissue may be seen between individual cells and groups of them."

As regards the origin of the tumors proper, a number have been definitely proven to be of epithelial origin, and therefore entitled to the name of carcinomata. The cases reported by the following men are now almost universally classed as of epithelial origin: Johnston, Gilchrist,[14] Waelsch,[15] Whitfield,[16] Darier,[17] Schalek,[18] and Ravogli.[19] Johnston comes to the following conclusions: (1) Aside from the natural division into choroid and skin tumors, melanotic neoplasms, which, from their diversity of origin, are best called melanomata, show several varieties. (2) The commonest, and therefore the most important, is that derived from the soft nevi, which are endotheliomata of lymph vessel origin. Nevomelanomata, whose histogenesis it is not possible to determine, must be referred to the same origin. (3) A second variety exists with the same histologic pictures, which does not spring from nevi, and whose origin is directly traceable to endothelium, probably also lymphatic. This group includes the melanotic whitlow and the malignant lentigo of the French. (4) A third division is truly epithelial in origin, although its existence has been denied. These tumors are of various types and show only very slight tendency to malignancy, a fact sufficient in

[9] Soldan: Arch. f. Klin. Chir., 1899, lix, 261.
[10] Borst: Die Lehre von den Geschwülsten, 1902, 117.
[11] Ribbert: Geschwülstelehre, 1904, 277.
[12] Adami: Principles of Pathology, i, 764.
[13] Johnston: Jour. Cutan. Dis., 1905, xxiii, 1.
[14] Gilchrist: Jour. Cutan. Dis., 1899, xvii, 117.
[15] Waelsch: Arch. f. Dermat. u. Syphil., 1900, xlix, 249.
[16] Whitfield: Brit. Jour. Dermat., 1900, xii, 267.
[17] Darier: La Pratique Dermatologie, iii, 1903.
[18] Schalek: Jour. Cutan. Dis., 1900, xviii, 147.
[19] Ravogli: Jour. Cutan. Dis., 1901, xix, 1.

itself to determine a cardial difference from the melanoendotheliomata, whose capacity in this direction can hardly be exaggerated. (5) A histological diagnosis is the only proper method of differentiation between the two. Adami says: "Pigmented tumors of a pure epitheliomatous type are unknown," but Fordyce thinks that he is mistaken in this.

To the author the following conclusions seem irresistible: (1) Nevoid cells have a twofold origin, one from the basal cells of the epidermis, and another, not yet determined, possibly from the endothelium. (2) Malignant melanomata of the skin spring directly

Fig. 49.—Low-power photomicrograph of a malignant pigmented mole (nevocarcinoma). (Author's collection.)

from these cells. (3) Melanotic sarcomata may spring from other organs, as from the choroid, the gall-bladder (Duval),[20] adrenal (Orth),[21] and many other organs. (4) Lymphangioendotheliomata are not nearly so malignant as these tumors (see chapter on endothelial tumors). (5) Basal-celled carcinomata are certainly not as malignant as this group. The whole question, then, is still unsettled, although it seems probable that some of these tumors are carcinomata and some sarcomata.

Microscopically, a fully developed tumor (Figs. 49, 50) shows

[20] Duval: Montreal Medical Jour., 1908, xxxvii, 270.
[21] Orth: Berlin klin Wchnschr., 1906, xxvi.

either an alveolar arrangement of large or small cells, bundles of spindle- and oat-shaped cells, or a combination of the two, the picture varying in different portions of the same tumor. The amount of chromatin varies; in some fields not only the cell nucleus may be obscured, but even the cell shape, while in other fields it is present in comparatively small amounts. Borst has pointed out that there was more pigment near the great blood vessels. The melanin, which is the pigment present, is in the form of fine amorphous granules, varying in color from a golden yellow to a very deep brown. It is generally conceded to be the final stage of the cell, and, where

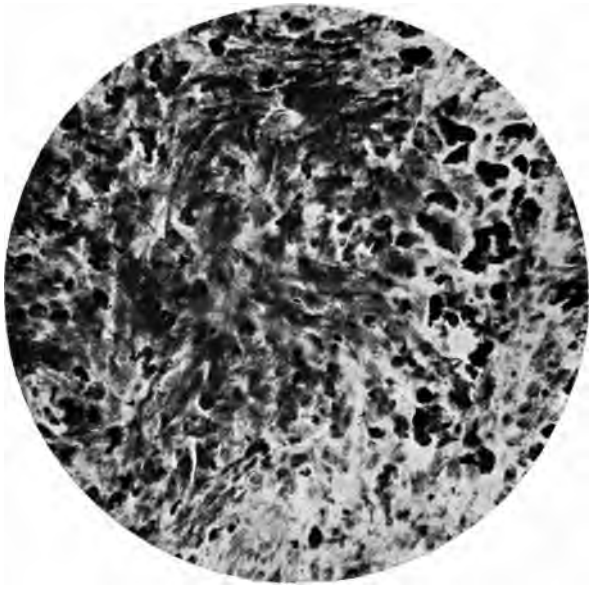

Fig. 50.—High-power photomicrograph of malignant mole. (Author's collection.)

there is most, the cell is the oldest or the best nourished. As regards the origin of the melanin, it is still undetermined whether it arises from the blood, or whether it orginates in the cutis or the epidermis.

Diagnosis.—As a general rule, the diagnosis of these tumors is only too easy, for they are rarely seen before metastases have occurred. In the author's experience two conditions have proven troublesome, which may best be illustrated by case reports. In the first instance a young girl consulted him because of a jet-black tumor that had developed upon the edge of an old vaccination scar. Examination showed a tumor about the size of a pea, firmly adherent

to the deeper layers of the skin, and with dilated blood vessels extending from it. It was completely excised with a wide margin, and microscopical examination showed that there had been a small venous angioma, into which hemorrhage had taken place some time before, and that the blood pigment had remained. The other case was somewhat similar. On the edge of the nostril there had developed a mass that was black in color, and the diagnosis of melanoma was made. Histological examination, as well as the later course of the disease, showed that the growth was inflammatory tissue into which hemorrhage had taken place with the deposit of blood pigment. Histologically, this case was very difficult to distinguish from a true melanotic tumor, and was watched with a certain amount of suspicion for some months.

Prognosis.—The prognosis is bad. Bloodgood[22] states that he has the record of but one case that has survived—a case of Dr. Wainwright, of Scranton, who is alive seventeen years after operation. The histological picture was such that the true melanotic nature of the tumor could not be doubted. Pringle[23] has reported two cures, which Bloodgood[24] does not accept. As a general rule, patients die inside of two years, but in a few instances life is prolonged well beyond that time. It is possible that in some few instances life might be saved by a very extensive early operation, an operation including the glands.

Treatment.—Prevention is much better than cure. Every acquired mole should be removed, preferably with either the knife or actual cautery, so as not to irritate the nests of nevoid cells. Every congenital mole that is subjected to irritation should be removed. Whenever a mole begins to grow, or to show any evidences of either irritation or ulceration, it is an imperative sign for immediate operative interference, although this will often be too late. When skin or internal metastases have manifested themselves, treatment is useless; neither Coley's serum, x-ray, nor radium will have the slightest influence. In the cases where the involvement is glandular only, either extensive block dissection of the glandular vessels and glands, or, if the growth be upon a limb, amputation might cure.

[22] Bloodgood: Progressive Medicine, Dec., 1912.
[23] Pringle: Edinburgh Med. Jour., June, 1908.
[24] Bloodgood: Progressive Med., Dec., 1909.

CHAPTER X.

CARCINOMA EN CUIRASSE—CARCINOMA BY EXTENSION—METASTATIC CARCINOMA—PAGET'S DISEASE.

CARCINOMA EN CUIRASSE.

Pollitzer[1] has recently written an excellent article on carcinoma of this type, and the author has drawn freely from it.

Just as in many other cancerous conditions, there are many degrees of involvement, and the author can see no reason for not calling even minor involvement of the lymphatics of the skin, causing induration, by the name of *cancer en cuirasse,* although many will not accept this view.

Clinical Course.—This type of cancer was first described by Velpeau about seventy-five years ago, and fully developed instances are very rare. The trouble probably always begins in the glands of the breast, notwithstanding the statements of Rodman and Besnier to the contrary. In a typical case we find a breast cancer, with retraction of the nipple, and possibly all of the other signs of a typical mammary carcinoma, although the skin of the gland may be so indurated that it is impossible to palpate the primary tumor. Beginning in the breast, and extending from it over the chest and back, to a greater or less extent the skin is reddened, very hard and firm to the touch and feeling like a sclerodermatous cutis (Fig. 51). There may or may not be very numerous small angular or round papules present, but there are usually a few. These papules may resemble the lesions of lichen planus to a marked extent. Pollitzer says that in his case the appearance was that of a lichen planus developing upon a sclerodermatous area. The glands may or may not be involved, and the disease usually runs a comparatively slow course, about that of a slow-growing scirrhous carcinoma. Owing to the obstruction of the lymphatics, the arm may become markedly edematous. At times there is very intense itching over the diseased area, and movement is usually greatly limited and at times painful.

Pathology.—The pathology of the condition is comparatively simple. Instead of passing through the lymph vessels, the cancer cells have grown into them in long, finger-like projections, almost com-

[1] Pollitzer: Jour. Cutan. Dis., 1909, xxvii, 143.

pletely filling the lumens. Very little of the cancerous tissue is found outside of the lymphatics. There is very little inflammatory reaction in the cutis; the blood vessels, glands and connective tis-

Fig. 51.—Carcinoma en cuirasse. (Sutton's collection.)

sue are unchanged. The lichenoid papules are due to a hyperacanthosis over three or four of the papillæ, and not to the deposit of cancerous cells in the more superficial portions of the skin. The erythema is probably due to the effect of the toxins upon the vasomotors in a region in which the flow of lymph is obstructed. Cer-

tain of the nodules that can occasionally be felt deeper in the skin are due to accumulations and growth of cancer cells that have escaped from the lymphatics and started to grow in the connective tissue.

Diagnosis.—The diagnosis must be made from erysipelas, scleroderma, and lichen planus, and should be easy, provided that a careful examination is made. Especially should the nipples be examined for retraction, and the lesions carefully palpated.

Treatment.—When this stage of cancer has been reached, the treatment consists simply in keeping the patient as comfortable as possible.

CARCINOMA BY EXTENSION.

Clinical Course.—Now that the public is beginning to more fully appreciate the danger of lumps or tumors in any part of the body,

Fig. 52.—Extension of carcinoma of the breast. (Author's collection.)

the surgeon does not often see a case with ulceration through the skin, except after an unsuccessful operation. Fungating tumors of the skin are probably commoner after cancer of the breast than after any other type of cancer (Fig. 52), although it is not unusual for lymph glands, infected with cancerous material, to break down and

form deep ulcers. Two clinical types of cancer by extension are seen—the fungating and the ulcerating. In the former a mass of papillomatous tissue extends through the skin. The color is somewhat that of dirty-looking granulation tissue, but always covered with a necrotic membrane. There is usually considerable discharge and the odor is very foul. In the ulcerating variety there is an ulcer of more or less depth, with a hard edge, dirty base, and a foul discharge.

Pathology.—The pathology, of course, depends entirely on the variety of antecedent tumor.

Treatment.—These conditions may at times be temporarily ameliorated by operation, but the chances for a permanent cure are very slim, although x-ray treatment has apparently cured a few, and radium promises something.

METASTATIC CARCINOMATA.

Clinical Course.—It is rare to find cancer of any of the organs metastasizing to the skin, but this does occasionally happen. Kaufmann-Wolf[2] has recently written a very complete article on the subject, and has collected all of the published cases, sixty-five in number. It is to this article that the author owes the following statements.

The condition is very rare. Riechelmann,[3] in autopsies upon 711 carcinomatous subjects, did not once encounter this condition, Buday[4] found it three times in 366 cases, while Krasting[5] mentions seven instances of cutaneous metastases in 1,078 carcinoma cases, four of these, however, being associated with mammary cancer.

Out of the sixty-five cases that Kaufmann-Wolf has collected, twenty-three followed cancer of the stomach; three cancer of the liver; two, cancer of the pancreas; ten, cancer of the uterus; one, cancer of the ovary; six, cancer of the lung; two, cancer of the mediastinum; two, cancer of the esophagus, while the remainder sprang from various other organs. Twenty-three of the patients were men; thirty-three were women, while in the other instances the sex was not stated. Many of the patients were extremely old, but some were comparatively young, so it is improbable that age is a factor.

In only one or two instances was there a solitary metastasis to the

[2] Kaufmann-Wolf: Arch. f. Dermat. u. Syphil., 1913, cxiv, 709.
[3] Riechelmann: Berl. klin. Wchnschr., 1902, 728, 758.
[4] Buday: Zeitschr. f. Krebsforschung, vi, 26.
[5] Krasting: Zeitschr. f. Krebsforschung, iv, 336.

skin; in the majority of instances the condition was simply associated with a general carcinomatosis. In the skin there are three forms of tumors—solitary nodules, groups of nodules, and a flat infiltraing form of neoplasm. The tumors are rather prone to early ulceration, except in those cases where the pathology showed the condition to be one of lymphatic infarction.

In some of the instances the patient died very soon after the appearance of the cutaneous manifestations, but the average duration of life after cutaneous metastases had taken place was about six months. One patient lived for one and a half years.

As accompaniments or prodromal symptoms there were found edema, herpes zoster-like vesicles, erysipeloid erythema, lichenoid conditions, and urticarial phenomena. With lymphatic infarction the edema was rather constant. Itching was often complained of.

Pathology.—The type of cancer found in the skin depends on the nature of the primary growth.

Treatment.—Treatment consists in keeping the patient comfortable.

PAGET'S DISEASE.

This condition was first described by Paget[6] in 1874, and since that time has been the subject of much study. Especially has it been debated whether the cutaneous changes antedated or followed the development of a cancerous change, and even yet this question is not absolutely settled.

Clinical Course.—Paget's disease usually begins as a peculiar raw, granulating, weeping eczematous patch around the nipple of a woman past middle life. Later the breast is noted to be the seat of cancer, and there is the same fatal termination so common in other instances of this malady.

The disease is, however, subject to many variations. In some instances, from a clinical standpoint, the cutaneous lesion is, very clearly, simply an example of a chronic, weeping eczema. In other instances the cancerous change undoubtedly antedates the skin changes. Hartzell[7] has collected nineteen illustrations of the occurrence of Paget's disease on other portions of the body than the breast. These extramammary cases are most common upon the penis, but, as Hartzell well shows, may develop upon almost any other portion of the body. In the discussion of Hartzell's paper it was generally agreed that it is not at all unusual to find these extra-

[6] Paget: St. Bartholemew's Hosp. Rep., 1874, v, 87.
[7] Hartzell: Jour. Cutan. Dis., 1910, xxviii, 379.

mammary cases, and nearly every dermatologist of wide experience has seen one or more.

In the breast cases the dermatitis may exist for as much as eight or ten years before the cancer is clinically demonstrable, and, inasmuch as cancer of the breast, when untreated, almost invariably runs a more rapid course than that, it is probable that the dermatitis is the original lesion, and is not secondary to the neoplasm, as Jacobeus[8] and others believe. The cancer does not, by any manner of means, always develop directly from the diseased skin, although it not infrequently does so, but in many instances it arises

Fig. 53.—Histology of Paget's disease. (Author's collection.)

at a distant point, and from the glandular epithelium and not from the cutaneous cells. In the extramammary cases the cancer develops from the skin cells, and usually in from two to three years after the dermatitis has manifested itself. It then runs the course of the more malignant prickle-celled neoplasms, not forming the typical rodent ulcers.

Pathology.—Pathologically, the condition is extremely interesting, owing to the presence of the curious Paget's cells, about which there has been much discussion (Fig. 53). It has been thought by some that they were simply modified epithelial cells, by Jacobeus

[8] Jacobeus: Arch. f. path. Anat. (Virchow's), clxxviii.

and others that they were in reality cancer cells growing up toward the skin from a deep-seated carcinoma, and by Darier,[9] Wickham,[10] and others to be parasites, the so-called psorosperms. Practically all pathologists have now conceded that the first view was correct, and that they are simply modified and degenerated prickle cells, derived from the epidermis.

The intrapapillary processes are much longer than usual, and are rounded rather than pointed. The cells are often widely separated, due to the presence of intracellular edema, and have lost their prickles. Some of the cells are as much as 30 microns in diameter, and usually contain a very large nucleus, lying in a vesicle. Other cells show similar, but not so marked, changes, which have been very well described by Unna.[11] There is a very considerable cellular infiltration, both of the rete and the adjacent portion of the corium. These changes are true, not only of the typical breast changes, but of the cutaneous cases as well.

Should the disease be regarded as a true precancerous condition, or as a disease *sui generis,* as maintained by Unna? In the extramammary cases it is probably an example of a true precancerous dermatosis, but, inasmuch as in the breast cases the cancer may develop at a distant site, it can hardly be assumed as a pathological precancerous change, but simply as a clinical entity that definitely warns that a deep cancer may follow. As a general rule, precancerous changes are dry and hard, and not moist and weeping as in Paget's disease.

Prophylaxis and Treatment.—At any rate, there is one very important lesson to be learned, a lesson that has as yet not been sufficiently emphasized. Any patient with an intractable eczema of the nipple region should invariably have a biopsy performed, and, if the sections show the changes characteristic of Paget's disease, that breast should be removed without any delay, for it will inevitably become cancerous. Whether the glands should be removed depends probably on the stage at which the operation is performed. If there is the slightest clinical evidence of cancer, a complete operation must be done, but, if clinical examination and the careful examination of the breast when it has been excised show no naked eye appearances of cancer, then the simple removal of the breast will suffice. However in all instances a microscopical examination of the removed tissue should be made.

The cutaneous cases should be treated in the same way. If they

[9] Darier: Soc. de Biologie, April 13, 1889.
[10] Wickham: Maladie de la peau dite maladie de Paget, Paris, 1890.
[11] Unna: Histopathology of the Diseases of the Skin.

are examples of extramammary Paget's they should be excised with a goodly margin.

Once cancer has developed, the prognosis is naturally unfavorable, as only a very extensive operation would give the patient a fighting chance for life.

CHAPTER XI.

ENDOTHELIOMATA.

Among pathologists there is still much confusion regarding the status of endotheliomas, and what tumors should be called by this name. In a recent article Fick[1] contends that the pathological entity known as endothelioma never has and never can exist, and that the so-called endothelial cells are in reality epithelial in origin, perhaps derived from some of the glandular elements. On the other hand, Zeit,[2] in an excellent article, maintains that many of the so-called alveolar sarcomata and carcinomata are undoubtedly examples of endotheliomata. This confusion is undoubtedly due to the variability of the cells. Zeit remarks: "Morphologically, an endothelioma may resemble typical (adenoma) or atypical (carcinoma) organoid structures, or typical (fibroma) or atypical (sarcoma) histoid growths. It is extremely confusing for the student who has learned how to diagnose common atypical histoid growths, as sarcomata and atypical organoid tumors as carcinomata or endotheliomata, to read of the diagnosis of an atypical organoid tumor by Billroth as alveolar sarcoma; by Rindfleisch as sarcoma endotheliale; by Waldeyer and Kolaczek as angiosarcoma; by Fischer and Cramer as endothelial sarcoma." And the author much fears that it is not alone the student who is confused, but even some of these very writers themselves.

Zeit goes on to say that a correct clinical diagnosis is of the greatest importance to the surgeon because endothelial tumors grow very much more slowly than sarcomata, and do not produce metastases until they have existed for some years. At the same time, they are very prone to recur after operative removal.

The following scheme of classification is usually adopted:

1. Lymphangioendothelioma.
2. Hemangioendothelioma.
3. Perithelioma.

The perithelial tumors originate from the endothelium lining the perivascular lymph spaces, and hence there is some discussion as to

[1] Fick: Dermat. Wchnschr., 1912, liv, 488.
[2] Zeit: Jour. Amer. Med. Assn., 1906, xlvi, 567.

whether they should be called hemangioendotheliomas or lymphangioendotheliomas, according to some authors.[3] On the other hand, Zeit emphatically says: "The perithelial membrane must be differentiated from the perivascular lymph spaces of His, which he found surrounding the adventitia of arteries, veins, and capillaries of the central nervous system. The perithelium is the outer lining of the adventitia of blood vessels, outside of which is the perivascular lymph space." Zeit further states that the true peritheliomata are the tumors arising from the perithelium and not from the lymph space, and hence should be called *hemangioendothelioma perivasculare.*

At any rate, up to the present time, there is in the literature but one definite case report of a perithelioma of the skin, and that is a case reported by Brandeis and Pouget,[4] where there were a number of metastases from a tumor of the adrenals.

From carcinomas the histological diagnosis can be made from carefully noting the following differences, according to Zeit:

1. "The tumor cells in endothelioma are intimately connected with the stroma, and cannot be brushed out of the stroma, as in the case of carcinoma, in which the epithelial cells may also retract from the stroma and show spaces.

2. "Endothelial cells produce intracellular cement substance and are closely packed together, whereas the epithelial cells in carcinoma have no intercellular substance and form no compact layers.

3. "In endothelioma delicate fibrillar processes extend from the walls of the alveoli into the proliferated cell masses. They are absent in carcinoma.

4. "In endothelioma the cell masses consist of a dense mosaic of many layers of cells, with small sharply-outlined nuclei, surrounded by a broad envelope of clear, glassy perinuclear protoplasm. Carcinoma cells have large vesicular nuclei, with a moderate amount of perinuclear protoplasm, more or less granular.

5. "In endothelial tumors the cells are arranged in the form of cellular cords and cylinders (round masses in carcinoma), and may separate out hyaline material (cylindroma) or form lumina-like masses (sieve-like) in the cellular cords, due to secretory processes of endothelial cells.

6. "To distinguish the endothelial tumors from sarcomata, it is to be remembered that the former have an organoid, the latter a his-

[3] Adami: Principles of Pathology, i, 758.

[4] Brandeis and Pouget: Ann. de Dermat. et de Syphil., 1910, 5th ser., i, 506.

toid, structure. According to this definition, every large-cell sarcoma with a well-developed stroma, which was formerly called alveolar sarcoma, would be called an endothelioma."

As Hertzler[5] well points out, however, there may be so many changes associated with an endothelioma that it is next to impossible for any one except a very highly trained pathologist to correctly diagnose it. There may occur a hypertrophy of both the number and size of the vessels involved, be they lymph or blood channels, or in other instances there may occur a great increase in the amount of fibrous tissue present between the cells. The cells may undergo marked degeneration, so as to almost resemble cancer pearls, except that the keratin is lacking. The vessels may or may not retain an open lumen.

Endotheliomas of the skin are very rare tumors, and such textbooks as Crocker, Hyde, Stelwagon, Pusey, and even Mracek's extensive *Handbuch* either make no mention of the condition, or else refer only to the so-called endothelioma capitis.

In 1907[6] Gottheil reviewed the literature, in addition to reporting a case of his own. He calls attention to the fact that the lesions have varied greatly in clinical characteristics, and that as yet we have no definite criteria by which they can be diagnosed with certainty.

Most of the lesions have appeared upon the scalp, either as single or as multiple tumors. In Braun's[7] case there was a solitary lesion that closely resembled a rodent ulcer, especially as the edge was markedly indurated. In the case reported by Allen[8] there was a single cartilaginous lesion, while in Hartzell's[9] case the neoplasm was softer and of a yellowish color. Von Waldheim[10] recorded an instance where there were multiple, flat, smooth tumors covered by unaltered epidermis. In the patient reported by Gottheil there was a solitary, deeply pigmented tumor, occurring upon the sole of the foot, and closely simulating a melanoma, except that the growth had been comparatively slow. It recurred about six months after removal by the knife. In the discussion on this case, Bulkley recorded a similar case upon the foot, which likewise recurred after operative removal, but which was finally cured by the x-rays. Dr. Cocks referred to a case which was clinically diagnosed as molluscum fibrosum.

[5] Hertzler: Treatise on Tumors.
[6] Gottheil: Jour. Amer. Med. Assn., 1907, xlviii, 93.
[7] Braun: Monats. f. prakt. Dermat., 1893, xvii, 585.
[8] Allen: Monats. f. prakt. Dermat., 1900, xxxi, 47.
[9] Hartzell: Brit. Jour. Dermat., Oct., 1904.
[10] von Waldheim: Arch. f. Dermat. u. Syphil., 1902, lx, 215.

The author has recently had a very interesting case under his own care. The patient was a maiden lady, aged 50, who had a small blood-red, somewhat friable, growth situated back of her right ear, where the spectacles had irritated it. The growth was about 8 mm. in diameter, was distinctly pedunculated, and there was no induration around the edge. It had been present about two months. On account of the rapid growth, the condition was diagnosed as a sarcoma, and was completely excised under local anesthesia, and the wound cauterized with acid nitrate of mercury. Five x-ray exposures were then given. There has been no recurrence in two years.

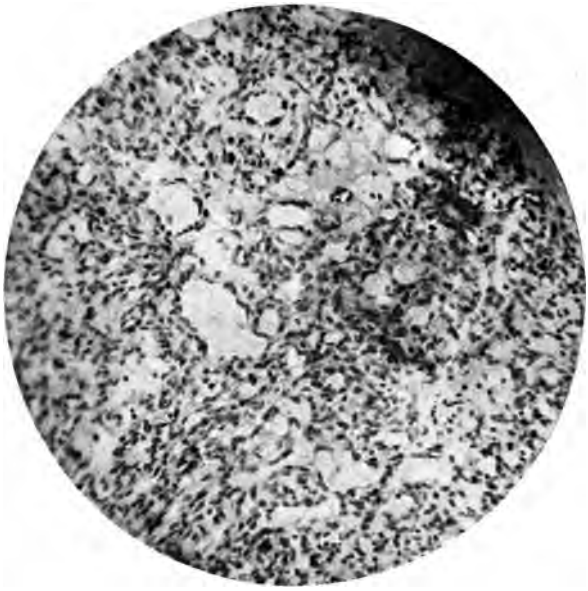

Fig. 54.—Histology of lymphangioendothelioma. (Author's collection.)

The growth was diagnosed microscopically as lymphangioendothelioma by Dr. Welch, of Johns Hopkins (Fig. 54).

The proper treatment is broad local excision, probably accompanied by cauterization, for the growths undoubtedly have a marked tendency to return at the site of the operation, although apparently they do not form metastases.

It must be especially noted that these growths have nothing whatever to do with the multiple, benign, cystic growths, properly called syringocystadenoma. Many authors insist that the latter are of endothelial origin, and within a short time Saalfeld[11] has attempted

[11] Saalfeld: Technical Supplement Urol. and Cutan. Review, 1913, i, 166.

to describe two varieties, one springing from the lymphatic endothelium, and one from the endothelium of the blood vessels. A careful reading of his article, however, must convince one that the origin was really in the epithelium of the sweat ducts, as in the case so well described by Sutton[12] and confirmed by Welch.

NEVO-XANTHO-ENDOTHELIOMATA.

McDonagh[13] has described several cases of small multiple, yellow tumors, present at birth, which were apparently distinct from xanthomata in that the histological examination showed that the cells were probably of endothelial origin. These neoplasms ran a totally benign course. They tend to disappear spontaneously.

[12] Sutton: Jour. Amer. Med. Assn., 1912, lviii, 333.
[13] McDonagh: Brit. Jour. Dermat., 1912, xxiv, 85.

CHAPTER XII.

BENIGN CONNECTIVE TISSUE TUMORS.

Before dealing with the sarcomata, it seems wise to say a few words concerning the benign connective tissue tumors, the sarcomata being the malignant connective tissue tumors.

CICATRIX.

A cicatrix, or scar, is a new formation of connective tissue, replacing a loss of tissue substance. The amount of scar formation depends, of course, on the preceding loss of tissue. As a rule, a scar contracts in the course of time, although hypertrophic scars may form. At first the color is bright-red, then dull-pink, then white, the color depending on the vascular supply. The pathology of the condition is admirably described in Adami's little book, "Inflammation."[1] As already pointed out in the chapter on spino-celled cancer, cicatrices may lead to the later development of prickle-celled cancer, but sarcomas may also develop in them.

KELOID.

A keloid is a fibrous new growth that, to all intents and purposes, is simply a hypertrophic scar. They are not especially common in whites, but are very frequently encountered in the negro. In former years it was believed that there were two varieties of keloid—the false, which arose as the result of trauma, and the true, which originated in a healthy skin. It is now generally conceded, however, that all keloids are the result of some injury, although it is by no means understood why the overgrowth of fibrous tissue should occur. Keloids may be single or multiple, and they may be very small or they may reach the diameter of 6 or even more inches. They may be either sessile or pedunculated. The growth is very hard and firm, and usually distinctly rounded, in addition to being definitely encapsulated. Keloids are devoid of hair.

Pathologically, the condition has been most carefully studied by Heidingsfeld,[2] who found that all hypertrophic scars and keloids were of similar structure, and composed of dense bands of fibrous

[1] Adami: "Inflammation," New York, 1907.

[2] Heidingsfeld: Jour. Amer. Med. Assn., 1909, liii, 1277.

tissue, usually running parallel with the surface. The epidermis is usually flattened and thinned. Glands, hair follicles, and muscles are pushed aside, and may be somewhat atrophied. There are but few blood vessels present. As a general rule, keloids do not become malignant, although Anderson[3] has reported a case where such change did occur. The best treatment for keloids is the x-ray; in fact, it is the only treatment that is at all satisfactory.

The acne keloid, or dermatitis papillaris capillitii, is a collection of small keloidal growths upon the back of the neck and upon the adjoining posterior portion of the scalp. Each papule is pierced by one or several hairs, and there is often pus in the follicles. The condition has recently been carefully studied by Adamson.[4] X-ray is the treatment of preference.

FIBROMA.

True fibromas of the skin are rather rare tumors, even in the negro race. They do, however, occasionally occur, usually as solitary tumors in adults. They are occasionally found upon the abdomen, arising from the sheaths of the recti muscles. Fibromata of the tendon sheaths are also sometimes encountered. The growths are usually small, sharply circumscribed hard nodules, that are round or oval in shape. Fibromas always have a certain tendency to degenerate into sarcomas, so should always be removed, preferably by excision.

FIBROMA MOLLUSCUM.

The fibroma molluscum, also called neurofibroma and von Recklinghausen's disease, is a tumor derived from the sheath of a cutaneous nerve. The growths are usually multiple, and are accompanied in many instances by telangiectases and pigmented areas. The subjects are frequently below par mentally. The growths are often rather soft to the touch, and they may be of a distinct violaceous color. They are occasionally very painful to pressure. The growths do not tend to disappear spontaneously; in fact, the reverse is often true, and malignant degeneration may occur in them. In some instances these tumors are solitary and are then pendulous, and often of great size. Surgery alone is useful in the treatment of this affection. Neither the x-ray nor radium have proven of any value in handling these lesions, nor has internal medication influenced them.

[3] Anderson: Lancet, 1888, i, 1025.

[4] Adamson: Brit. Jour. Dermat., 1914, xxvi, 69.

NEUROMA.

According to Heidingsfeld,[5] very few cases of neuroma cutis have been described. In the cases reported by this author and in others which he has gathered from the literature, the tumors were usually solitary, but were rarely multiple, and appeared clinically as subcutaneous nodules that could readily be mistaken for either fibromas or myomas. Pressure upon these growths, however, usually gave rise to lancinating pains. Histologically, examination revealed the presence of nerve tissue, sometimes associated with either muscle or endothelial tissue. Surgical intervention was curative.

MYOMA.

This rare tumor of the skin has been carefully studied by Heidingsfeld.[6] The growths may take their origin from the muscle normally present in the walls of the vessels, in the arrector pili muscles, or in the muscular attachments to the glands. Clinically, they are subcutaneous single or multiple tumors that are apt to be painful upon pressure. In some instances they are associated with cavernous dilatation of the blood vessels. They can be diagnosed with certainty only by microscopical examination. Surgical intervention is curative.

LIPOMA.

Lipomas or fatty tumors are probably the commonest benign tumors that are encountered in surgical dispensaries. They sometimes develop in children, but much more commonly in adults. The solitary forms are much commoner than the multiple or diffuse. They may be found upon any portion of the body. They vary greatly in size, from being almost microscopic to a weight of several pounds. They have their origin in the subcutaneous fatty tissue. There are several types—the solitary, the multiple, and the diffuse. The latter condition is often spoken of as "fatty neck." Lipomas do not become malignant, and are not dangerous in any sense, but are rather unsightly. They may be easily removed by surgical interference, and do not recur if completely removed.

OSTEOMA.

True bony tumors of the skin must be differentiated from calcareous deposits which are the result of chronic inflammatory proc-

[5] Heidingsfeld: Jour. Amer. Med. Assn., 1913, lxi, 405.
[6] Heidingsfeld: Jour. Amer. Med. Assn., 1907, xlviii, 562.

esses. Heidingsfeld[7] has briefly reviewed some of these cases in addition to reporting one of his own. The growths probably arise from congenitally misplaced bone cells. The growths are always small, and usually occur in connection with other lesions. Histologically, they show typical bone structure. They may be removed by operation.

HEMANGIOMA.

A hemangioma or vascular nevus is a congenital new growth and hypertrophy of the blood vessels of the skin. Small telangiectases are frequently acquired, but the larger lesions are always congenital. Unna is inclined to believe that external pressure during intrauterine life is responsible, while still others have thought that nerve changes might be responsible, inasmuch as they frequently develop along the distribution of a nerve.

Several groups must be recognized. First, the small telangiectatic spots; second, the flat nevi; third, the nevi containing spongy tissue of a somewhat erectile character and that protrudes considerably above the surface of the skin; and fourth, the racemose aneurysms. The second class usually remain stationary, but the members of the other three groups may grow to a considerable extent, so should always be kept under observation. Occasionally a sarcoma may develop from one of these lesions.

The smaller telangiectases can be removed, if this be considered advisable, by either the electric needle or by carbon dioxide snow. The pale flat nevi should be left alone, and even the dark ones are difficult to handle satisfactorily, although many claims have been made for the Kromayer lamp, claims that not all dermatologists are willing to concede. Radium is not satisfactory, as it acts by producing scar tissue. Mild freezing with carbon dioxide snow is at times beneficial. The large protruding nevi are probably best treated by means of the snow, this being undoubtedly much better than injections of boiling water or scarification with the cautery. The racemose aneurysms should be treated by surgical methods.

LYMPHANGIOMA.

As Stelwagon[8] well points out, the subject of lymphangioma is still a rather confused one, inasmuch as no hard and fast dividing line has been drawn between actual new growths and lymphangiectases.

[7] Heidingsfeld: Arch. f. Dermat. u. Syphil., 1908, xcii, 337.
[8] Stelwagon: Diseases of the Skin, 7th ed., 661.

Lymphangiectases may be observed in either the superficial or deep lymphatics. The superficial form appears as minute or slightly larger vesicles, which, when ruptured, give a discharge of lymph. The deep variety is usually secondary to some inflammatory process, and can be recognized only as a corded growth beneath the skin.

Simple lymphangiomata occur as circumscribed, slightly elevated tumors, consisting of enlarged lymphatics. The forms best known are in the tongue or lip, the former being known as macroglossia and the latter as macrochelia.

Lymph cysts are deep cystic tumors that come under the domain of surgery.

Lymphangiomata may be the seat of a latter sarcoma, so should always be removed when possible.

LYMPHANGIOMA CIRCUMSCRIPTUM.

This disease is characterized by a hypertrophy and new growth of lymph capillaries, characterized by circumscribed, elevated, crowded vesicles filled with lymph. As a general rule, the disease begins early in life, so may be due to a congenital defect. As a general rule, there is but one patch present, and this usually occurs upon the limbs, neck, or upper portion of the body. The vesicles are firm and not easily ruptured. The pathology has been well studied by Gilchrist.[9] These lesions can be easily removed with the actual or electric cautery.

[9] Gilchrist: Bull. Johns Hopkins Hospital, 1896, 138.

CHAPTER XIII.

SARCOMATA AND SARCOIDS.

SARCOMATA.

The subject of sarcomata of the skin is still in a greatly confused condition. It is not yet definitely known whether the multiple pigmented growths are derived from the epithelium or from the mesoblastic structures, and neither is it definitely decided whether many of the alveolar growths are endotheliomata or sarcomata. Again, the dividing line between the sarcomata and certain so-called cases of mycosis fungoides and lymphoid tumors is a very shadowy one, and, last, certain cases of sarcomata cannot be definitely distinguished from certain of the sarcoid tumors. Until these growths can be distinguished, or until they can all be proven to be merely different forms arising from the same cause, the subject must of necessity remain hazy.

In a short chapter of this kind it seems best not to attempt to reconcile all of these differences, but rather to point out that they do exist, and to describe the well-known and typical forms of this very serious type of cutaneous neoplasm.

The following classification is tentatively adopted:

Sarcomata.
- Solitary lesions.
  - Round-celled.
  - Spindle-celled.
  - Giant-celled.
- Multiple lesions.
  - Round-celled.
  - Melanotic.
  - Pigmented hemorrhagic (Kaposi).
- Transitional type.
  - Spiegler-Fendt sarcoids.

Sarcoids.
- Boeck type.
- Subcutaneous type of Darier and Roussy.
- Nodular type on extremities.

SOLITARY LESIONS.

Round-Celled.—The small round-celled sarcomata are extremely malignant; for it is a peculiarity of sarcomata that the nearer they approach the embryonic type of cell in structure the more malignant they are.

Incidence.—The lesions are relatively uncommon, and the majority of dermatologists have not seen more than half a dozen cases. The disease only rarely arises *de novo;* it usually commences in the scar of a burn, in a nevus, either vascular or pigmented, or in some other abnormality of the skin. Bloodgood,[1] in discussing the etiology of sarcomata of the skin in general, states: "Among forty cases of sarcoma of the skin there was a distinct precancerous lesion in thirty-two. These lesions were as follows: Congenital nevi, six; scars, nineteen; fibromas, seven." Bloodgood further states that the more malignant tumors, which he is pleased to call perithelial angiosarcomata, but which are probably to be classed under the oat-shaped-celled heading, frequently develop from a congenital nevus, trauma usually starting the new growth. In every instance a fungous tumor develops, usually very rapidly.

Clinical Course.—Clinically, there are two types of tumor—(1) where a nodule apparently begins in the normal skin, and (2) where a nevus breaks down. In the first type it is noted that a pale-red, rather vascular, nodule begins to protrude from the skin, and that it bleeds very easily on injury. The lesion is usually round at the start, and may project above the skin, or may be beneath it, according to the depth of the tissue from which it sprang. Ulceration usually takes place, in the center of the growth at least. In the deep type there is considerable induration, but not of the stony character so typical of carcinomata. Growth may be slow or very rapid, and metastasis to the glands often takes place within a few weeks after the first appearance of the tumor is noted. It is not infrequent to find a few metastases in the neighboring skin.

Pathology.—Pathologically, the cells are either small or large round cells (Fig. 55) that may or may not be divided into islands by fibrous tissue. Mitotic figures are very common. Usually there is but little inflammatory exudate around the edges of the invading growth. Unna[2] has some very interesting ideas as to the origin of the sarcoma cells. He holds that the degeneration begins in the healthy tissue with a swelling of the spindle cells; these cells soon

[1] Bloodgood: Progressive Medicine, Dec., 1912.
[2] Unna: Histopathology of Diseases of the Skin.

withdraw their processes, become round or cubical, and often form true plasma cells. From them, near the margin of the new growth, the true sarcoma cells develop. Thus the plasma cells are a stage in the development of round-celled sarcoma from spindled-celled mesoblastic structures.

Diagnosis.—The sarcomata of this type must be distinguished from endotheliomata, granuloma pyogenicum, and various adenomata of the skin structures. In case of doubt the new growth should be removed by a broad excision, and submitted to histological examination. Usually, however, diagnosis is not difficult, for in sarcoma the growth is more rapid, and there may be early ulceration of the skin.

The sarcomata, originating from nevi, resemble the group first

Fig. 55.—High-power photomicrograph of small round-celled sarcoma of skin. (Author's collection.)

described, except in their origin and early appearance. At first it is noticed that the nevus is enlarging, and ulceration speedily takes place. Then a fungous tumor usually protrudes from the area of ulceration, and the further course is as already described.

Prognosis and Treatment.—The prognosis is bad. Bloodgood states that only one of his six cases was cured by operation. Operation should consist of wide local excision, and removal of the neighboring glands at the same time, using a block operation, so that all tissue is taken out in one place.

Spindle-Celled.—The spindle-celled sarcomata are much commoner than are the round-celled neoplasms for the reason that mesoblastic tissue is normally composed of spindle cells. Different

grades of malignancy exist, according to whether the tumor consists of fibro-spindle cells, or of the pure oat-shaped or spindle cells.

Incidence.—This group of tumors frequently arises from the scars of old wounds or burns, especially those that have healed slowly. Bloodgood states that he has never seen a malignant neoplasm arising from a wound that has healed by first intention. These tumors sometimes arise from preexisting fibromata.

Clinical Course.—The tumors appear as firm white or pinkish growths, that usually grow rather rapidly. There is usually considerable dilatation of the surface blood vessels, and ulceration takes place early. The neighboring glands usually become involved within one year. At times, when a glandular enlargement is found, this is not due to metastases of the sarcoma cells, but to inflammation.

Pathology.—Pathologically, the cells consist of various types of spindle cells. In some cases these approach fibrous tissue in character, and in other cases are short and oat-shaped: the latter are much more malignant. These cells are arranged in bundles that intersect the growth at all angles, and forming a sort of frame around the blood vessels, which are dilated. Some blood pigment may be deposited in the tissue, chiefly around the vessels. Mitotic figures are rarely seen. A few plasma cells are usually found scattered among the spindle cells, chiefly near the edge of the growth. The elastic tissue is lost at once and the normal lymphatics are obliterated. There is no inflammatory reaction as occurs in carcinoma. Certain of these tumors undoubtedly have their origin in the blood vessels, and hence deserve to be called angiosarcomata, but all tumors of this class do not arise in this way. For a fuller discussion of the pathology of these neoplasms the reader is referred to the work of Unna, which is very complete, and gives an excellent bibliography.

Diagnosis.—This group of tumors is easy to diagnose, largely because of the early ulceration.

Prognosis.—The prognosis is much better than in the other variety of sarcomas, although by no means as good as might be desired. Bloodgood states that in nineteen cases six have remained well after operation, although most of these were fairly well advanced cases. If the cases can be operated upon early, at least 50 percent should be saved.

Treatment.—If seen early, a broad local excision, probably with oval of the neighboring glands, should be the method employed.

Neither radium, the x-ray, nor any of the caustics should be used, except in inoperable neoplasms.

Giant-Celled.—Giant-celled sarcomas of the skin are extremely rare, although a few instances have been recorded.

Unna reports a case where there was a small, bluish-red, angioma-like tumor of the face. Unna says: "The whole cutis was transformed into a tumor mass, with numerous cells and very little intercellular substance, over which the epidermis was here and there thinned, and in one place ulcerated. . . . It was evident that the tumor cells developed from spindle cells, which, by taking up protoplasm, at first around the nucleus, enlarged, and then assumed all possible forms and dimensions. The cells are so multiform that it is hardly possible to describe them. . . . Almost all of them contain several nuclei. They passed very gradually into giant cells, with which every section swarmed."

Pasini[3] has recently reported a case of giant-celled sarcoma of the skin, and both Crocker[4] and Perrin and Leredde[5] have reported instances of sarcomatosis of the cutis from giant-celled neoplasms. These last reports seem rather singular, for *a priori* one would hardly suspect that a growth showing the characteristics of a giant-celled sarcoma would be so malignant. In other regions they certainly are not.

Treatment.—The treatment should consist of ample local excision, and not of caustics or x-rays, except perhaps as an adjunct to the knife.

As regards the local treatment of extensive or inoperable sarcomata, but little can be said. Wickham has had some really remarkable results with radium. Those who have seen the photographs that he exhibited at the International Dermatological Congress held at Rome in 1912 were wonderfully impressed with his success. A few good results from the x-ray have been reported, but they have not been constant. So far as general treatment goes, Coley's[6] serum should be tried, although Coley has had rather better results than others who have used the preparation. Coley's serum consists of a vaccine made from the streptococcus of erysipelas and the bacillus prodigiosus. The rationale of the treatment is as follows: Some years ago it was noted that when a patient suffering from sarcoma was attacked by erysipelas, the result upon the neoplasm was most beneficial; this led some clinicians to inoculate their hopeless sar-

[3] Pasini: Gior. Ital. d. Mal. Ven. e. d. Pel., 1912, liii, 353.
[4] Crocker: Diseases of the Skin.
[5] Perrin et Leredde: Ann. de Dermat. et de Syphil., 1895, vi, 1038.
[6] Coley: Amer. Jour. Med. Sc., 1893, cv, 487; 1906, cxxxi, 375.

coma patients with erysipelas, but the results of the infection were frequently so disastrous that Coley determined to try vaccines, and in some instances his results were excellent. Coley himself does not advise the use of the serum upon operable cases.

Fig. 56.—Multiple sarcomata. (C. J. White's collection.)

MULTIPLE LESIONS.

Round-Celled.—Sarcomatosis of the skin, except with melanotic growths, is very unusual. When this condition does occur, it is

usually with the small round-celled type of neoplasm, for this is the most malignant variety. The following may be taken as a typical example: Patient was a white man aged 41, who had always enjoyed the best of health until six months previously, when small nodules began to appear upon his scalp, shortly followed by their development upon trunk and limbs. Examination revealed a healthy looking, strongly built man who looked the picture of health. All over his body there were, however, at least two hundred small cutaneous and subcutaneous nodules, usually about 1 cm. in diameter, but a few were 4 to 5 cm. in diameter. There was no ulceration of the skin over them. Tumors were freely movable in the skin, and were rather firm to the touch. There was no marked dilatation of the surface vessels. In the groin there were a number of enormously enlarged glands. Excision of one of the small growths showed a typical small round-celled sarcoma. In other instances the tumors are much fewer in number and may be comparatively large. It is rare to find a spindle-celled sarcomatosis of the skin except in tumors of the multiple hemorrhagic variety. The outlook is hopeless; neither Coley's serum nor x-ray has any effect, and patients usually die within a year.

Melanotic.—The multiple melanotic growths, so frequently called melanotic sarcomata, have already been described in another chapter.

Pigmented Hemorrhagic (Kaposi).—The multiple pigmented hemorrhagic sarcoma of Kaposi[7] is rather a curious lesion in many respects, for it lacks the malignancy of a true spindle-celled sarcoma, although composed of that variety of tissue; at times it seems to heal spontaneously, and may be related to the sarcoid group of tumors.

Incidence.—The disease is rather rare in both England and America, although cases in the latter country have been described by Fordyce,[8] Hyde,[9] Hartzell,[10] and others. In continental Europe it is much commoner. Kaposi has had over thirty cases, De Amicis[11] in Italy over fifty, and many have been reported from Austria and Russia. In America it occurs most commonly in Jewish immigrants, which might seem to speak for its infective nature.

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[7] Kaposi: Kaposi and Hebra, Dis. of Skin, New Sydenham Soc. Translation, London, 1875.

[8] Fordyce: Jour. Cut. and Gen. Urin. Dis., 1891, ix, 1.

[9] Hyde: Quoted by Crocker.

[10] Hartzell: Jour. Cut. Dis., 1908, xxvi, 97.

[11] De Amicis: Il Morgagni, 1872.

Clinical Course.—The affliction always begins on either the hands or feet, usually the dorsal surface. At first an edema is noted, then bluish spots appear, in the center of which are nodosities. The tumors slowly increase in both size and number, usually traveling up the limb. The neoplasms are either round or flat, are dark-red at first, then purple, and then brown. The color is due to hemorrhage and the deposit of blood pigment. They vary in number from twenty to several hundred, and in size from 1 cm. to 15 cm. (Fig. 57). They may be hard or soft, and usually bleed readily when punctured. The general health is not affected for several years, and in the early stages there is no glandular involvement. The patients ultimately die from general sarcomatosis. Mariani[12] has given the best survey of the subject, including literature, yet extant. It is to be noted that these tumors grade off into the Spiegler-Fendt type, usually called sarcoids, and also described by Polland as comparatively benign sarcomata.

Pathology.—Histologically, there may be seen numerous large cavities filled with blood, the space between the cavities being composed of parallel rows of spindle cells, between which is deposited much pigment. Traces of hemorrhages may be seen in places. This picture has been interpreted by some as the result of infection—that is, that the tumor is in reality a granuloma—and by others as a pure sarcoma of a special type, the latter view predominating.

Treatment.—Treatment is not satisfactory. According to Köbner,[13] Sherwell,[14] and De Amicis, arsenic will cure some cases if given in large amounts and over a considerable space of time, Fowler's solution being the form generally employed. Possibly cacodylate of soda, used intramuscularly, might produce a better effect, and yet one must be inclined to agree with Fox and Wile, who believe that arsenic cures only sarcoids and not true sarcomata. X-ray is useful in certain cases, though probably not for any great length of time. One observer has reported the disappearance of the lesions following the local application of bichloride solutions.

TRANSITIONAL LESIONS.

Spiegler-Fendt Type.—Tumors of the variety described by Spiegler,[15] Fendt,[16] Polland,[17] and others, and commonly called the Spieg-

[12] Mariani: Arch. f. Dermat. u. Syphil., 1909, xcviii, 267.
[13] Köbner: Berl. med. Wchnschr., 1883, No. 2.
[14] Sherwell: Amer. Jour. Med. Sc., Oct., 1892.
[15] Spiegler: Arch. f. Dermat. u. Syphil., 1894, xxvii, 163.
[16] Fendt: Arch. f. Dermat. u. Syphil., 1900, liii, 213.
[17] Polland: Arch. f. Dermat. u. Syphil., 1910, civ, 69; 1912, cxi, 69.

ler-Fendt type of sarcoid, seem to occupy an intermediate position between the Kaposi type of multiple sarcoma and the comparatively harmless sarcoids.

In this group of lesions are purplish-red tumors, usually lying

Fig. 57.—Multiple hemorrhagic sarcoma (Kaposi). (Heidingsfeld's collection.)

deep in the cutis, essentially chronic in course, showing no ulceration, and almost invariably giving no metastases, although Spiegler has reported one fatal case. Histologically, there are more or less circumscribed areas of small round-celled infiltration. These aggregations may be inclosed in a connective tissue capsule. At times a few giant or epithelial cells may occur. Fox and Wile[18] very pertinently remark: "It is highly probable that many, if not all, of the so-called cured cases of sarcomatosis cutis belong to this group, which is really distinguished from true sarcomatosis cutis by the extreme malignancy of the latter and its tendency to invade the inner organs."

SARCOIDS.

The rather lengthy articles by Fano[19] and Darier[20] are extremely helpful in dealing with the problem of the border line conditions between the sarcomata and sarcoids.

Boeck Type.—The Boeck[21] type of sarcoid is probably the best known and the most often diagnosed. It may occur as one or more large nodules, as numerous papules, or in infiltrated placques, usually developing upon the face, back, shoulders, or arms. There are practically no subjective symptoms, and the general health is unaffected. The nodules are pink or purplish in color, and often show dilated peripheral vessels, and there may be slight scaling. To the touch they are firm and elastic, but there is no deep infiltration. The lesions run a chronic course and never ulcerate. They may involute spontaneously.

Histologically, the sections show sharply circumscribed, deep-seated nodules, composed of epithelioid cells, filling the perivascular lymph spaces. At the periphery one may observe lymphocytes and a few giant and plasma cells. There is no evidence of caseation necrosis, although Boeck considered the lesions to be tuberculous in origin.

The lesions involute under prolonged administration of arsenic.

Subcutaneous Type of Darier and Roussy.—The type of sarcoids described by Darier and Roussy[22] is rare and occurs only upon the trunk. There are found lesions of about 1 to 5 cm. in diameter, distinctly round or oval. The nodules are composed of epithelioid

[18] Fox and Wile: Jour. Cut. Dis., 1911, xxix, 375.
[19] Fano: Arch. f. Dermat. u. Syphil., 1907, lxxxiii, 33, 225, 427.
[20] Darier: Monatsh. f. prakt. Dermat., 1910, l, 419.
[21] Boeck: Jour. Cutan. and Gen.-Urin. Dis., 1899, xvii, 543.
Arch. f. Dermat. u. Syphil., 1905, lxxiii, 71.
[22] Darier et Roussy: Ann. de Dermat. et Syphil., 1904, v, 144, 347.

cells and lymphocytes and numerous giant cells. The changes are less circumscribed than in the Boeck type, and at times seem to be distinctly infiltrating.

Nodular Type on Extremities.—The last type, suggested by Darier, resembles the erythema induratum of Bazin; in fact, the following name has been suggested, "sarcoides noueuses et nodulaires des membres." The lesions usually develop upon the legs of adult women, and present reddish or purplish nodules or infiltrations. It is very difficult to separate this group from true cases of erythema induratum, especially as this type of sarcoids may occasionally ulcerate.

Darier especially points out that all cases of sarcoids do not run true to form, and that one case may show features of several of these groups, either clinically or histologically.

Etiology.—In regard to etiology, there are two views—one that the affection is of tuberculous origin, and the other that it is not. In favor of the tuberculous etiology may be cited the microscopic findings, the epithelioid and giant cells, although the author by no means admits that the presence of giant cells makes a diagnosis of tuberculosis certain, for they can be found in almost any chronic inflammatory condition of the skin, even down to acne vulgaris. Winckler,[23] in an analysis of seventeen cases, found evidence of tuberculous deposits in the body in six cases, and that about ten cases out of thirty-one reacted positively to tuberculin, a figure not much more than the general average of supposedly healthy persons. A positive inoculation experiment has been recorded by Morawitz.[24] On the other hand, Kren and Weidenfeld[25] made inoculation experiments in two cases with negative results. Histologically and clinically, there is no evidence of cascation or necrosis, which fact is very unlike those usually observed in tuberculosis of the skin. Arsenic will cure sarcoids and will not cure tuberculosis.

Diagnosis.—From the standpoint of differential diagnosis, it is at times extremely difficult to exclude sarcomatosis cutis, only the course of the disease serving to do that. Leukemia cutis, leprosy, and syphilis can be differentiated by the various laboratory tests in case of doubt.

Prognosis and Treatment.—The prognosis for both life and the local betterment is good. Arsenic has a remarkable effect, although it must frequently be used over a long space of time. Darier thinks that the x-ray, calomel, and tuberculin are also useful.

[23] Winkler: Arch. f. Dermat. u. Syphil., lxxvii, 3.
[24] Morawitz: Arch. f. Dermat. u. Syphil., 1910, cii, 121.
[25] Kren and Weidenfeld: Arch. f. Dermat. u. Syphil., 1909, xcix, 79.

CHAPTER XIV.

LYMPHOMATA.

The subject of lymphoid and myeloid tumors has long confused not only dermatologists, but clinicians and pathologists as well. It seems to the author, however, that certain broad principles are now clear, and that all that is needed is to study the details. Adami's[1] classification of the lymphoid and myeloid diseases is possibly the most satisfactory one, inasmuch as it is the simplest and most comprehensive, although he does not follow Türck[2] in dividing lymphomatoses into leukemic and aleukemic, and pointing out that certain of the former type should become converted into the latter variety, which should always be borne in mind.

The following group of diseases is associated with cutaneous tumors:

Myelomata.
- Multiple myelomata.
- Myeloid leukemia.
- Chloroma.

Lymphomata.
- Hodgkin's disease.
- Lymphatic leukemia.

In addition to these general diseases, lymphomatous processes may be at first localized in the skin and only later involve the other blood-producing organs. The primary lymphatic diseases involving the cutis are simple lymphomata, mycosis fungoides, and lymphodermia perniciosa. The general field has been reviewed by the author[3] in two recent articles, one in association with Strobel,[4] in which there is a full discussion of the problems here encountered as well as a complete bibliography.

Multiple Myelomata.—Two cases of multiple myelomata showed cutaneous manifestations. The patient of Spiethoff's showed only an erythrodermia, but Bloch's[5] case had definite tumors of 5 cm. size.

[1] Adami: Principles of Pathology, i.
[2] Türck: Wien. klin. Wchnschr., 1903, xvi, 1073.
[3] Hazen: Jour. Cutan. Dis., 1911, xxix, 521.
[4] Strobel and Hazen: Jour. Cutan. Dis., 1911, xxix, 147.
[5] Bloch: Arch. f. Dermat. u. Syphil., 1910, xcix, 9.

Myeloid Leukemia.—Only three cases of myeloid (splenomyelogenous) leukemia showed tumors, although two or three others had various types of skin lesions. Hindenberg had under observation a woman aged 40 with a well-developed myeloid leukemia and a tumor of the leg 6 cm. in diameter, which was distinctly due to the leukemia. Rolleston and Fox[6] followed a patient aged 58 with an atypical myeloid leukemia and many nodules over the body. Bruusgaard has had a case in which there were infiltrations of myelocytes in the subcutis.

Chloroma.—In all, ten cases of chloroma showed cutaneous manifestations, five of these patients had tumors or nodules, usually of a greenish color—namely, the cases of Rosenblath, Bramwell, Hitschmann, Paltauf,[7] and Jacobaeus. The nodules were usually of small size, and freely movable upon the underlying tissues. The most characteristic thing was the greenish color.

Hodgkin's Disease.—Hodgkin's disease still remains a fertile field for contention. After Reed's[8] work appeared it was thought for a time that this malady was definitely established, and that it was characterized by a very definite histological picture. Cases have, however, been reported where a perfectly typical case of this trouble has developed into an equally typical leukemia, and Warthin[9] has shown that certain cases have the pathology of simple lymphomata, and not of the type described by Reed. In this disease the commonest skin manifestations are either bronzing or pruritus, but definite nodules or tumors may develop.

Lymphatic Leukemia.—Lymphatic leukemia is fairly sharply divided into the acute and chronic forms, although there are, of course, transitional stages between these two varieties.

The patients suffering from acute leukemia frequently showed purpuric conditions of the cutis, a number of other cases showed either vesicles or urticaria, but seven cases showed either nodules or small tumors. These cases are described in the author's article as well as in the more recent one of Nanta.[10]

Patients suffering from the chronic form of lymphatic leukemia not infrequently show papules or vesicles upon the skin, but nine cases have shown either tubercular eruptions or fairly large tumors. As a rule, these lesions did not ulcerate, but one or two have done so. Thick subcutaneous infiltrations were not uncommon; these

[6] Rolleston and Fox: Brit. Jour. Dermat., 1909, xxi, 377.
[7] Paltauf: Mracek's Handbuch der Hautkrankheiten, Wien., 1909, v.
[8] Reed: Johns Hopkins Hospital Reports, 1902, x.
[9] Warthin: Osler's Modern Medicine, Phila., 1908, iv, 808.
[10] Nanta: Ann. de Dermat. et de Syphil., 1912, iii, 572, 639, 694.

occurred usually upon the face, and often gave the patient a leonine expression, such as is seen in leprosy.

Lymphodermia Perniciosa.—Lymphodermia perniciosa[11] is undoubtedly a transition stage between leukemia and mycosis fungoides. Typical cases of this affection show an intensely itchy, generalized erythrodermia, that resembles a generalized squamous eczema. Later cutaneous and subcutaneous nodules and infiltrations develop, that may or may not ulcerate. The majority of these cases show a great increase in the white blood cells, the lymphocytes being the most numerous cells.

Mycosis Fungoides.—Mycosis fungoides is one of the most interesting diseases encountered by the dermatologist. According to Crocker,[12] it appears in three different forms—first, where there is an antecedent dermatitis, usually eczematous in appearance (Fig. 58); second, where there are repeated attacks of lymphangitis leading to elephantiasis, and a later tumor formation; and third, where many tumors suddenly appear without an antecedent dermatitis, the "tumeurs d'emblee" of the French.

This disease has variously been classed with the sarcomata, the infectious granulomata, and the lymphomata. In a careful study of the condition, Strobel and the author decided that the malady was not a true sarcoma for the following reasons: that the cells do not infiltrate or metastasize in the way that sarcoma cells do because the tumors usually develop from placques or papules (which is certainly not true of the sarcomata); because of the spontaneous disappearance of the eruption at times; and because of the sudden changes that might take place in it. Nor did the histological picture appear to be the same.

They felt that it could not be an infectious granuloma because of the richness of mitotic figures in the mycosis cells; because the rete was not invaded by these cells; because there was no attempt on the part of the body to wall in these cells by an inflammatory exudate or fibrous tissue; because the clinical course and fatal termination of the disease are different from those of the granulomata; because there is no history of contagion or any especial geographical center for the trouble. In a certain number of cases lesions have been described in the bone marrow or in some of the internal lymphatic structures, never elsewhere, which could hardly be true of the granulomata.

They especially felt that the disease should be classed with the lym-

[11] Kaposi: Diseases of the Skin, New York, 1895.
[12] Crocker: Diseases of the Skin, 3d ed., Phila., 1905.

phomata because of the histology of the growths, the lesions consisting of lymphoid cells; because the disease has the same general

Fig. 58.—Mycosis fungoides. (Strobel and Hazen.—Courtesy of Journal of Cutaneous Diseases.)

characteristics as many others of the lymphoid and myeloid series —namely, that it usually occurs in males past 49 years of age; that the average duration is two to five years, and that death invariably

comes; that there is a secondary anemia, and that the lymphocyte count may be very high, usually showing an increase in the large mononuclear cells; and that a typical leukemia may develop as in the case reported by Pardee and Zeit;[13] and, lastly, that there are direct transitional stages between the leukemias and mycosis fungoides, as evidenced by the conditions known as lymphodermia perniciosa. Also, it should be remarked that the same remedies have a beneficial effect here as in the other members of the group—namely x-ray and arsenic—and also intercurrent infections, especially erysipelas. They, therefore, feel that mycosis fungoides is a member of the group of diseases usually called lymphomatous, and that, in the sense of Türck, it is an aleukemic lymphomatosis, that may, however, become leukemic.

Diagnosis.—In this entire group of troubles diagnosis should not be difficult if it is possible to study the patient. The laboratory methods of diagnosis are extremely valuable, for the diagnosis of leukemia can always be made by a microscopical examination of the blood, if it be borne in mind that a victim of leukemia may have an occasional aleukemic period. Mycosis fungoides can be diagnosed by the study of a section of the skin. Even the premycotic patches have a very definite histology, there being an infiltration of the subpapillary portion of the corium with lymphoid and an occasional endothelioid or plasma cell. Even the supposedly normal skin may show some of these changes. In multiple myelomata there is a large quantity of Bence-Jones bodies in the urine. A typical case of Hodgkin's disease can be diagnosed by a histological study of a small lymphatic gland. The following conditions must be excluded; leprosy, sarcomata, sarcoids, fibroma molluscum, and small subcutaneous or cutaneous tumors of benign course, such as myomata or neuromata.

Treatment.—The treatment is eminently unsatisfactory. Arsenic or the x-ray may alleviate the trouble for a time, but the author is not satisfied that any genuine cases belonging to this group have been cured, although there have been a few reports in the literature. He is inclined to feel that these cases probably belong to the Spiegler-Fendt type of sarcoid.

Benign Lymphomata.—Not all lymphomata, however, are malignant, for Winfield[14] has recently reported a remarkable case of benign lymphomata occurring in a woman aged 75. The disease started six years before the report was made as two subcutaneous

[13] Pardee and Zeit: Jour. Cutan. Dis., 1911, xxix, 7.
[14] Winfield: Jour. Cutan. Dis., 1913, xxxi, 245.

nodules over the left malar prominence, that were intensely itchy. Both tumors grew rather rapidly until they attained the diameter of about 2 cm., but they did not coalesce, nor did the skin over them ulcerate. A little later similar tumors began to appear on other portions of the face, and upon the body and limbs as well. Careful physical and laboratory investigations yielded no information as to disease in any of the internal organs. Histological examination of the lesions showed a nodule, well walled in and not invading the epidermis, the cells being of a small, round character, greatly resembling those of a small round-celled sarcoma, or of a lymphosarcoma; they were, however, later decided to be typical lymphoid cells. Some of the growths involuted under the administration of arsenic.

Newberger reported a somewhat similar case in 1892, where there were likewise small, hard growths in the corium, without any other symptoms.

In addition to the articles mentioned above, Arndt's[15] should be read by any one who is interested.

[15] Arndt: Jour. Amer. Med. Assn., 1914, lxiii, 1268.

CHAPTER XV.

DIFFERENTIAL DIAGNOSIS.

In dealing with cutaneous neoplasms, there are two essentials—first, to decide whether the new growth is an inflammatory one or a true neoplasm, and, second, to decide whether, if it be a true tumor, if it be malignant or benign. If it be malignant, it is necessary to further decide whether it be a prickle-celled tumor, or a basal-celled growth, or if it be a sarcoma.

In order to decide this question accurately, it is often necessary to approach the problem in three different ways—first, the clinical aspects of the new growth; second, its gross pathology as seen by the naked eye; and third, its histological structure as seen by the microscope. The better the pathologist that the operator is the more frequently will he be able to make a diagnosis from the first two of these criteria, and hence the more promptly will the patient be dealt with and the necessity for second operations lessened.

History.—The first point is to obtain a careful history from the patient. The age must always be noted. It is rare for malignant epithelial tumors to arise before the age of thirty, except in the condition known as xeroderma pigmentosum. Nor does a mole often become malignant under the age of forty. Likewise, sarcomata of the skin are not common in the young.

The occupation of the patient must always be noted, for malignant tumors of the basal-celled variety not infrequently develop in those who have been much exposed to actinic rays, whether produced by the sun or by the röntgen tube. Those who are engaged in the manufacture of paraffin and tar are especially liable to cutaneous cancer.

Furthermore, it should be decided whether there was a precancerous dermatosis antedating the new growth. From the common senile warts we usually find a basal-celled carcinomata resulting; from an x-ray burn a prickle-celled neoplasm is much more likely to arise. If the growth be from a pigmented mole, we are usually dealing with either a nevocarcinoma or multiple melanomata, both very malignant. In the scars of old wounds prickle-celled growths or sarcomata may arise, while from vascular nevi we practically find only sarcomata.

The duration of symptoms is likewise of special import, for the more malignant the tumor the more rapidly it grows. A basal-celled tumor may grow more rapidly than a prickle-celled one, but this is rare.

With a deeply seated neoplasm it is always best to exclude syphilis, and, to decide on this point, the patient's word should never be accepted, but the diagnosis confirmed by the various laboratory tests, remembering that both the Wassermann and luetin reactions may be negative in long standing cases of this malady, and hence not putting too much reliance in them. At times a superficial gumma before ulceration may almost exactly resemble a nodular or rolled-edge rodent ulcer.

The symptoms of onset must be noted, and what was the first, pain, itching, serous discharge denoting superficial ulceration, or the presence of a nodule. It must always be remembered that pain is comparatively rare in skin tumors, whether malignant or benign.

The later symptoms must be carefully asked for in order to determine as to the possibility of metastases. While cachexia is extremely rare in skin cancers, yet metastases from them may cause these symptoms. In large ulcerating growths the absorption of toxins from secondary bacterial infection may cause a picture of cachexia.

The local signs and symptoms are much more important than the general; we must always try to find out how rapidly the tumor grew when first observed, and how rapidly it has grown within the past few weeks.

Examination.—In the examination of the growth, certain facts must be observed. First, we should note the relation of the tumor to the skin, for certain tumors arising from the appendages may not at first be adherent to the epidermis, while the basal- and prickle-celled growths almost invariably are attached to the skin from the incipiency. On inspection we must note the size of the growth—whether it is exuberant or whether it has formed a deep ulcer. The character of the surface must be observed, for prickle-celled neoplasms usually have a very rough and irregular surface. The amount and character of the discharge is important, for absorption may cause many general symptoms. Metastatic growth, either in the vicinity or in the glands, must be looked for. And especially important is the situation of the tumor, for growths on the face except the lips are usually comparatively benign, while those upon the extremities are usually very malignant. Likewise, if there be multiple growths, they are probably of a basal-celled origin, if not examples of multiple sarcomata.

On palpation the character of the induration is especially important, for the carcinomata invariably have an extremely hard edge, while in inflammatory lesions this is lacking as a general rule. The depth of the induration is likewise important, for in the malignant growths this is usually considerable. It must always be borne in mind that there may be an inflammatory induration that may simulate a cancerous one. The neighboring glands should always be palpated, again remembering that an enlargement of them can denote an inflammatory condition.

Gross Pathology.—After a tumor is excised, it should be sectioned at once in order to determine its variety and the depth of its infiltration. In the squamous-celled cancers the infiltration is comparatively deep and wide. These growths also show a characteristic picture on section, for there can be observed fine white lines, about the size of fine sewing cotton, radiating downward from them, a condition totally lacking in the inflammatory conditions, and usually not marked in the basal-celled growths, where the cancerous alveoli are smaller.

In obtaining material for microscopic study, certain precautions must always be observed. Among the majority of surgeons there is a strong feeling that it is frequently dangerous to excise a portion of a tumor for examination if that tumor be of a malignant nature, for incision leaves a number of gaping blood vessels and lymphatics into which cancer cells might escape and thus cause metastases. At the same time, it is occasionally essential to examine such tissue, so the following scheme is usually adopted. If the tumor be upon the lip, or upon a part where it is possible to temporarily constrict the blood vessels by pressure, an assistant does this with his fingers, then a piece is excised under local anesthesia from the edge of the growth, taking care to include a small portion of apparently normal skin, in order to determine the infiltrative powers of the cancer cells, and the wound is then thoroughly cauterized with either the actual cautery or a strong chemical one.

In very early cases it is often impossible to determine from a clinical examination or from the naked eye appearance of the tumor to what variety it belongs, and then the whole growth may be removed and sections made from it.

Microscopic Pathology.—The tissue can be preserved in any of the accepted fixing agents, although 50 percent alcohol or 10 percent formalin will usually suffice, and is then fixed, blocked, cut, stained, and mounted in the usual manner. Probably, for routine examination, no stain is better than hematoxylin and eosin. A com-

petent microscopist can usually then diagnose the condition without trouble, although one should be selected who knows the difference between the basal- and prickle-celled varieties. In certain growths originating from the glandular appendages of the skin it is sometimes very difficult to decide whether the growths are malignant, and here it is occasionally necessary to have the services of an expert, and then opinions may differ. Usually, however, the question can be decided by any one who has had a broad pathological training. It must always be borne in mind by the novice that inflammatory conditions can cause a great overgrowth of epithelial tissue

Fig. 59.—In certain chronic infections of the skin, notably tuberculosis, of which this is an example, there is a marked hypertrophy of the epidermis, which may render it difficult to distinguish from cancer. Usually, however, the relationship between the basal- and spino-cells is not altered. (Author's collection.)

(Fig. 59), but this should not be mistaken for malignant hypertrophy, for the papillary structure is better retained; the cells of the rete are normal in arrangement and in their relationship to one another, even though they be greatly increased in number. Nor is the basement membrane broken through.

The microscopic differences between the squamous- and basal-celled types of cancer has already been fully discussed in the chapters dealing with those subjects.

In general, it may be said that four classes of lesions must be differentiated from the various types of cutaneous cancer—first, those lesions causing nodules, as the benign tumors, cysts of various kinds, chancres, and gummata; second, the ulcerative variety of lesions, as lupus vulgaris, syphilis in the primary or tertiary stage, traumatic ulcers, and certain of the rare granulomata, as sporotrichosis; third, the papillary lesions, such as a more or less diffuse papillomatosis secondary to irritating discharges, exuberant granulation tissue, granulomata pyogenicum, tuberculosis verrucosis, blastomycosis, and very rarely framboesiform syphilis; fourth, lesions causing scarring, as lupus vulgaris, syphilis, lupus erythematosis, and morphea.

Fig. 60.—Chancre of the chin. (Gilchrist's collection.)

1. Nodular Lesions.—There are, of course, many varieties of solitary tumors of the skin; there are found fibroids, fatty tumors, lymphoid tumors, neoplasms originating from the blood or lymph vessels, endotheliomata, wens, dermoid tumors, sarcoids of various varieties, and a number of inflammatory conditions, of which chancre and gummata are the more prominent. With the exception of the last two just named, the diagnosis is usually easy, for we find that nearly all of these growths present themselves as definitely encapsulated, slowly growing tumors, that only rarely ulcerate through the skin, and then only after they have existed for many years. All of them lack the stony hardness at the edge that is characteristic of the carcinomata, and also the firm attachments to the underlying

and overlying structures. Sarcomata may more nearly resemble these growths, for at first they are often found to be pretty definitely encapsulated, and hence freely movable.

Chancre.—At times it is extremely difficult to make a differential diagnosis between a chancre and a rapidly growing nodular cancer (Figs. 60, 61), for both have the same cartilaginous resistance, and ulceration often takes place in the center of each in about the same way. The observance of a number of facts will, however, aid in making a diagnosis. In the first place, the age of the patient is a great factor, for cancer is infrequent in the young, while chancre usually does not occur in the old, although it may, of course, do

Fig. 61.—Chancre of the lip of one month's duration. (Author's collection.)

so. Second, the location of the growth is of some aid, for chancres are rare except upon the penis, lips, or fingers, although they may, of course, occur upon any part of the body. Cancer is rather rare upon the upper lip, and practically never occurs upon either lip in a woman. Third, the growth of a chancre is usually very much more rapid than that of a cancer, a diameter of 2 cm. being not infrequently obtained in less than two weeks; and fourth, the neighboring glands usually swell within a month after the initial appearance of a specific lesion, which is not found in cancer. In cases of doubt, the spirochete should be searched for with the dark field illuminator; this instrument is much more satisfactory than the examination of stained specimens. Where none of these methods are

available, salvarsan should be administered intravenously, and, if the growth disappears, it was undoubtedly luetic.

Gumma.—Rarely a gumma may present symptoms that make it practically impossible to differentiate from cancer. The author has recently seen two cases of tumors upon the nose, both occurring in people past 40, who presented no other evidences of syphilis (Fig. 62). In both of these cases there was a raised, extremely hard edge, with dilated blood vessels, no ulceration for a number of months, and no marked inflammation present. Both cases were considered to be cancerous, but in both cases sections showed a typically gummatous structure, and both cleared up under salvarsan. As a general rule, a gumma is inflammatory and soon breaks down, forming a punched-out ulcer that has a soft edge (Fig. 63). There are three ways of making a differential diagnosis in doubtful cases—first and surest,

Fig. 62.—Gumma of the nose, with a hard-rolled edge simulating carcinoma. (Author's collection.)

by taking a piece of tissue for examination; second, by finding other signs of syphilis, either clinically or by laboratory methods; and last, by the so-called therapeutic test—namely, the intensive administration of antisyphilitic treatment.

2. Ulcerative Lesions.—The ulcerative lesions are usually easy to differentiate, for they too lack many of the physical characteristics of cancer—namely, the hard edge, with the pearly nodules therein.

Lupus Vulgaris.—Lupus vulgaris (Fig. 64) usually originates in the young; it is very rare to find a case starting in a patient over 20 years of age. The growth of the ulcer is slow, although not slower than that of a rodent ulcer. One characteristic of a tuber-

culous ulcer is the overhanging edge of skin, the ulcer not being cleanly punched out (Fig. 65). In some instances healing may take place in the center, leaving a comparatively superficial soft scar. A section taken from the edge of a patch of lupus will show that the condition is an inflammatory one, and the presence of giant, but more especially endothelioid, cells may be characteristic. The edge is never stony hard. It is surprising to see how often rodent ulcers are diagnosed as lupus, for in reality there is no excuse for this mistake.

Chancre.—A chancre rarely ulcerates extensively enough to be

Fig. 63.—Gummatous lesion of the lip. No induration at edges. (Author's collection.)

mistaken for an ulcerated cancer; it is only in the nodular type that trouble may arise.

Syphilis.—Syphilitic ulcerations, especially of the serpiginous type, where growth is slow at times, can be mistaken for an extremely superficial rodent ulcer, but the condition of the edge should serve to differentiate between them, for the syphilitic lesion does not have the great hardness and comparatively deep infiltration of the cancerous one. A biopsy would decide the question beyond all shadow of doubt, for syphilis, in its histological aspects, does not simulate cancer.

Traumatic Ulcers.—Traumatic ulcers lack the hardness of can-

cer, although they may become cancerous under very exceptional circumstances. A rapid growth of papillomatous tissue resembling a dirty granulation tissue, but more anemic and less vascular, would make one very suspicious of beginning malignant change. The same holds true of varicose ulcers.

Sporotrichosis.—The lesions of sporotrichosis[1] are usually multiple, and follow the course of the lymphatic vessels; in addition

Fig. 64.—Lupus vulgaris, showing spontaneous healing in center. Eight years' duration. (Author's collection.)

the causal organism can be demonstrated. Most of the other granulomatous affections are acquired in tropical or semitropical countries, and in persons who have lived in them such conditions must be excluded, which is usually not difficult, for the condition of the edge of the growth is a sure sign to guide one.

3. Papillary Lesions.—Most of the papillary lesions should not

[1] Hyde and Davis: Jour. Cutan. Dis., 1910, xxviii, 321

cause trouble, but occasionally they do, especially to one who has not seen many of them.

Diffuse Papillomatosis.—One condition that is not generally recognized even by experienced clinicians is the diffuse papillomatosis of the skin caused by an irritating discharge. Fig. 66 shows a very extreme form of it, but it is often seen in milder forms, especially around chronic leg ulcers in which there has been much weeping. The common venereal warts are the most familiar examples of this condition; other illustrations are the so-called dermatitis vegetans and pemphigus vegetans, in both of which conditions a discharge has set up a proliferation of epithelial tissue.

Fig. 65.—Tuberculous ulceration. (Randolph's case.)

Exuberant Granulation.—Ordinary exuberant granulation tissue is occasionally mistaken, but should not be, for it is of a different color, lacking the dirty-white splotched appearance that cancerous tissue assumes, and also totally lacking the induration.

Granuloma Pyogenicum.—The condition known as granuloma pyogenicum[2] is simply an excess of granulation tissue caused by an infecting microorganism, and might be confused with sarcoma, but

[2] Wile: Jour. Cutan. Dis., 1910, xxviii, 663.

never with carcinoma; the extreme tenderness and lack of induration in the growth should serve to differentiate it from either condition.

Fig. 66.—Diffuse papillomatosis of skin. (Author's collection.)

Tuberculosis Verrucosa Cutis.—Tuberculosis verrucosa cutis (Fig. 67) could be mistaken only by a tyro, for, as a general rule, the surface epithelium is almost intact, the lesions lack depth and induration, and are almost invariably multiple.

Blastomycosis.—Blastomycosis[3] (Fig. 68) usually causes a true papillomatous overgrowth of the skin; between the verrucose projections are minute abscesses containing pus, in which it is usually easy to demonstrate the causative organism. The color is often purplish, and there is a lack of deep infiltration, the condition feeling soggy, rather than indurated. The lesions are usually multiple, and there may be a number of minute abscesses in the skin beyond the limits of the lesions proper.

Fig. 67.—Tuberculosis verrucosa cutis. (Author's collection.)

Yaws and Syphilis.—In either yaws or frambesiform syphilis the lesions are invariably multiple and lack deep induration; they are apt to be most pronounced on the face and around the genitalia or axillæ.

4. Scar-forming Lesions.—As already pointed out, cancer may heal spontaneously in the center, and have only a slight amount

[3] Stelwagon: Diseases of the Skin, 7th ed., Phila., 1914.

of ulceration at the edges; the most extreme example of this type is the morphea-like epithelioma. There are a number of other conditions which likewise cause scarring, perhaps with very little ulceration, and they must be diagnosed from this variety of cancer.

Lupus Vulgaris.—Lupus vulgaris will often heal in the center, and show only a comparatively narrow zone of ulceration at the margin. The overhanging edges of skin and the lack of deep induration would serve to distinguish this condition from cancer, even if the age of the patient did not, for lupus is extremely rare except in childhood.

Syphilis.—The lesions of syphilis spread very much more rapidly than do those of superficial cancer, and the ulceration is usually clean and punched out in appearance, besides lacking hardness.

Fig. 68.—Blastomycosis. (Author's collection.)

Lupus Erythematosus.—Lupus erythematosus causes scarring without ulceration; the surface of the skin is covered by closely adherent white scales, and the follicles gape widely; the color is pinkish. The lesions are usually multiple, have a great tendency to be symmetrical upon the face, especially the nose, cheeks, and around the ears. This condition may be confused with syphilis, but not of cancer.

Morphea.—Morphea may simulate one type of cancer, already fully described under the heading of morphea-like epithelioma in the chapter on the basal-celled cancers. As pointed out at that time, the presence of ulceration or of a raised firm edge should suffice to differentiate between them. Rarely the cancer *en cuirasse* may

resemble a scleroderma, but examination of the breast will usually clear up the diagnosis.

Serodiagnostic Methods.—It is impossible to conclude a chapter on the diagnosis of cancer without a word or two of reference to the attempts at laboratory diagnosis by means of utilizing the changes in the bodily cells and fluids that have taken place because of cancer. The majority of these tests are satisfactorily described in the third edition of Müller's "Serodiagnostic Methods," translated by Whitman.[4]

The reaction of Freund and Kaminer[5] depends on the observation that the blood serum of normal individuals has the power to dissolve cancer cells, the serum of cancer patients lacking this power —indeed having the power to inhibit the destruction of such cells by normal serum.

Von Dungern[6] has attempted the diagnosis by the well-known principle of deviation of the complement, but in the hands of others the results have not been satisfactory.

Kraus, Graff, and Ranzi[7] have attempted to diagnose cancer by means of the cobra venom method, which depends on the principle that in certain conditions human blood serum possesses the ability to activate the hemolysis of horse's red blood cells by cobra venom.

Marcus's[8] modification of the method of Müller and Jochmann[9] depends on the fact that the digestive power of trypsin is neutralized by a certain amount of serum or blood. The method of Bergmann and Meyer[10] depends on the same principle.

The meiostagmin reaction, as practiced by Ascoli and Izar[11] and others depends on the principle that, when diluted blood serum of patients is mixed with a homologous antigen and heated, there occurs a specific lowering of the surface tension.

Elsberg, Neuhof, and Geist[12] have described a skin reaction for carcinoma that has been investigated in this country by Lisser and Bloomfield[13] at the Johns Hopkins Hospital. The injection of 5 minims of a 20 percent suspension of washed human red blood cells

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[4] Müller: Serodiagnostic Methods, 3d ed. (translated by Whitman), Phila., 1913.
[5] Freund and Kaminer: Wien. klin. Wchnschr., 1911, xxiv, 1759.
[6] Von Dungern: Münch. med. Wchnschr., 1912, lix, 65, 1098, 2854.
[7] Kraus, Graff, and Ranzi: Wien. klin. Wchnschr., 1911, No. 28.
[8] Marcus: Berl. klin. Wchnschr., 1909, No. 4.
[9] Müller and Jochmann: Münch. med. Wchnschr., 1909, Nos. 29, 31.
[10] Bergmann and Meyer: Berl. klin. Wchnschr., 1908, No. 37.
[11] Ascoli and Izar: Münch. med. Wchnschr., 1910, lvii, 62, 182, 392, 403, 842, 1170, 2129.
[12] Elsberg, Neuhof, and Geist: Amer. Jour. Med. Sc., 1910.
[13] Lisser and Bloomfield: Bull. Johns Hopkins Hospital, 1912, xxiii, 356.

just beneath the skin is followed by a characteristic reaction in many cancer patients.

Even more recently it has been proposed to use a modification of the Abderhalden reaction for pregnancy.[14]

Fortunately, however, in cancer of the skin it is not necessary to depend on such methods, for the diagnosis can usually be made by inspection, and, if not, by the examination of tissue, which is always readily obtained.

[14] Editorial: Jour. Amer. Med. Assn., 1913, lxi, 1461.

CHAPTER XVI.

PROGNOSIS.

The prognosis in cancer of the skin depends on several factors—first, the type of cancer; second, the stage of the disease; third, the situation of the tumor; and last, the skill of the physician who has charge of the case.

Precancerous Conditions.—In the majority of instances the various so-called precancerous conditions and benign tumors do not become malignant, with a few exceptions. Xeroderma pigmentosum always becomes malignant, and cutaneous horns are very apt to do so. Probably from 5 to 10 percent of all senile keratoses, especially when situated upon the face, develop into cancers. When one considers the enormous number of pigmented moles that exist, it is evident that a very small percentage of them cause trouble, except when subject to chronic irritation, and then the percentage cannot be very high. The so-called nevi, including the pigmented ones and the very vascular ones, very rarely become malignant, but occasionally do. On the other hand, the lesions resulting from tar irritation and from the x-rays very frequently undergo cancerous degenerations. Inflammatory lesions only exceptionally become malignant; perhaps more cases of lupus vulgaris undergo this transformation than any other inflammatory conditions. The common leg ulcers very exceptionally degenerate.

And yet it must be remembered that every abnormality of the skin is a potential cancer, and that cancer practically never originates except upon the site of some pathological condition, be it congenital or acquired.

Prickle-Celled Cancer.—In cases of prickle-celled cancer, even upon the lip or penis, the prognosis is good if the cases are seen early and if a complete operation is then performed. Bloodgood[1] states that 40 percent of all cases of prickle-celled cancer, no matter if situated upon the tongue or other mucous membranes, and no matter how extensive, have been cured permanently at the Johns Hopkins Hospital. And Bloodgood does not consider a case cured if it remains alive six months after operation; he is more exacting. In early cases of cancer of the lip at least 90 percent should be

[1] Bloodgood: Amer. Jour. Med. Sc., 1914, cxlvii, 76.

cured by a complete operation, and about 70 percent of the late cases. In cancer of the other portions of the skin of the body a very high percentage should be cured if taken in time, and, in considering all classes of cases, the percentage of cures should be well over 50 percent.

Cuboidal-Celled Cancer.—In Bloodgood's series of cuboidal-celled growths the percentage of cures was only 33 percent, but this included many tumors of all stages and locations. If seen early, the percentage of permanent cures should be much higher than that of the squamous-celled neoplasms.

Baso-Celled Cancer.—Of the baso-celled growths 70 per cent have been permanently cured, and these figures include even the inoperable cases. When the growth is not over 2 cm. in diameter, 100 percent should be cured by a sufficiently radical treatment. In the more advanced cases, or where there is invasion of some of the natural openings of the face, the outlook is not so good, but nevertheless is not always hopeless by any manner of means.

Sarcoma.—In regard to sarcoma, Bloodgood furnishes us with some most interesting statistics. In six cases of "perithelial angiosarcoma" arising from a congenital nevus, there was but one cure; in eight similar cases, but arising *de novo,* there was not one cure. Twenty cases of sarcoma developed in scars; of these eight were cured, five lost track of, and the reminder not cured. "In every one of these cases the growth in the scar had continued one or more years, so that in every case there was sufficient clinical indication for an earlier intervention. Now, if the probability of a cure be 50 percent in late intervention, we can be quite sure that it will be much greater in early intervention." In nine cases of sarcoma of the skin there was a history of a preexisting fibroma, and only five of these cases have remained well.

The multiple sarcomata vary in malignancy. In the small round-celled cases the outlook is hopeless, but in the Kaposi and Spiegler-Fendt types the outlook is better, although most of the patients having the Kaposi variety eventually die, yet the patient may survive for a number of years.

Nevocarcinomata.—The nevocarcinomata and the melanomata are usually hopeless from the onset, for metastases have usually taken place by the time the patient notices the first change in the mole.

Cancer of Cutaneous Appendages.—The prognosis in the cancers arising from the various appendages of the skin, as well as the endothelial group, is fairly good, for a sufficiently broad local incision will usually cure both of these conditions.

Development.—The stage of the disease has, of course, a most important bearing, for an early prickle-celled cancer is much easier to treat and has a much better outlook than a very advanced basal-celled neoplasm. With the exception of the nevocarcinoma group, the prognosis of all early tumors is good, for every tumor is curable in some stage of its existence. Even in fairly well-advanced growths of almost any variety the prognosis is not absolutely hopeless if the tumor is so situated that a complete operation can be performed.

Location.—The location of the neoplasm is very important in determining the outcome, as well as the utility of the organ involved. In cancer of the face there is an unfortunate tendency to do too limited an operation because of the fear of deformity. Upon the eyelids or ears a complete operation is not only difficult, but very deforming. Upon the lip the prognosis is generally good, for, as already stated, the figures from Mayos show that over 80 percent of the early cases can be permanently cured, and about 70 percent of the late and recurrent cases give good results if submitted to a radical operation.

Tumors situated upon the limbs or body can usually be cured even at a fairly late stage, for here a large operation can be done with the more than fair chance of removing all of the cancerous tissue, even if some of it be in the lymphatic glands. Upon the penis the outlook is not so good, for cure demands the complete removal of that organ and of the neighboring lymphatic glands, and even then only about half of the early cases are cured. In the rare tumors of the basal-celled variety the outlook is much better, for local removal will generally cure.

Operator.—The skill of the operator is essential. In the first place, the surgeon or dermatologist should be able to accurately diagnose his case before operation, preferably without the use of a biopsy, for, as already pointed out, a biopsy may be dangerous, inasmuch as it may allow cancer cells to escape into the cut blood vessels or lymphatics. In some cases it is impossible to diagnose a growth until the time of operation, and then a surgeon should be sufficiently skillful as a gross pathologist to immediately tell what the character of the tumor is, and hence how extensive an operation is necessary.

Complete operations should be done in one sitting, for second operations are always dangerous for two reasons—first, because of the effect upon the general health of the patient, and second, there must of necessity be a break in the chain of complete

removal, and a few cells may be left at the dividing line between the tissue removed at the different operations.

In addition to this, the surgeon must know just how much tissue to remove and just how to remove it, as well as understanding how prolonged an ordeal the patient can stand.

It is frequently the fault of the physician that the growth is not removed at an early date; the diagnosis of cancer must always be proven or disproven as soon as the growth appears, and the expectant plan of treatment usually leads to very bad results. Fortunately the profession has awakened to the danger of the so-called precancerous conditions, and the laity, as a result, are much better informed than they formerly were. Every surgeon has commented on the number of patients suffering from still benign afflictions of the skin applying for advice and treatment. This one fact is the most hopeful sign that we have today as to the possibilities of permanent results in the field of cancer therapy.

Cancer Quack.—The so-called cancer quack is one of the menaces that today faces the public. The quack is in the field simply for the money that he can secure from unfortunate patients, and in 99 percent of the cases he is absolutely without conscience as to the manner in which he secures this. He is perfectly willing to tell a patient that any kind of a lesion is cancer and needs immediate and expensive treatment; he is absolutely ignorant regarding pathology, and makes no attempt to keep track of his results, except in the hope of securing more money. It is surprising to see how many of the hospital patients have had treatment from this group of men, and then eventually submit to a grave operation because of the loss of time.

In conclusion, the results in the treatment of skin cancer are much better than they formerly were, and will become much better as advice is sought earlier.

CHAPTER XVII.

PROPHYLAXIS.

Discovery of Cancer.—Until the true cause of cancer is discovered it will be impossible to prevent it in a truly scientific and effective way, and hence it is very necessary that the etiology be completely worked out. Fortunately there are a number of laboratories now established that are endeavoring to solve this difficult problem, and there is no doubt that some day one of them will succeed. Such a research, however, requires funds, and it is absolutely necessary that these institutions be supported.

The establishment of the various societies, both for educational purposes and for various types of cancer research, is one of the hopeful signs of the times, for the public must be educated to the point where they will seek advice before the cancerous stage is reached.

Precancerous Dermatoses.—In a more or less general sort of way we know that cancers of the skin are almost invariably preceded by some variety of precancerous condition, be it congenital, inflammatory, or neoplastic. In the first place, it is evidently necessary to prevent these precancerous dermatoses whenever possible, or at least to remove them if they be present. Chronic trauma of the skin or mucous membrane should be prevented, jagged teeth should never be allowed to remain, care should be taken to prevent burns of the lip resulting from the use of the pipe, cigar, or cigarette. This means that a fairly long stub should always be left if a holder is not used. There is no doubt that cigarette smoking can cause a precancerous dermatitis, although this fact is not dwelt on in the literature. Nor should the skin or any part of the body be chronically irritated, either by articles of clothing or by any instrument of trade. One should not persistently rub his body against a desk or table; those doing manual labor should protect themselves against trauma by suitable pads. A truss for hernia may cause cancer by its incessant friction and pressure. A suspender buckle may do the same thing; in fact, the possibilities are manifold.

Occupation.—As already pointed out, certain industries more than predispose to cancer of the skin. Schamberg[1] and others have shown

[1] Schamberg: Jour. Cutan. Dis., 1910, xxviii, 644.

how prevalent this condition is in those who are forced to handle the various products of tar and petroleum. Chimney sweeps were formerly liable to cancer of the scrotum. Complete cleanliness would doubtless save some men from industrial cancer of this nature. The majority of industrial cancers are, however, undoubtedly due to excessive actinic rays, either of the sun or of the x-ray, the latter being much the more dangerous. Those who are exposed to such dangers should take suitable precautions, lead being the material easiest to handle that is impervious to the Röntgen rays, and some sort of a mask sufficient to protect from the sun's rays.

Congenital Deformities.—While it is generally recognized that cancer may follow in the wake of various congenital deformities of the skin, still there is a widespread feeling that operative interference of any kind as applied to such a congenital defect is very dangerous and apt to cause cancer. This is a grievous error. Bloodgood[2] states that he has removed with the knife 175 clinically benign pigmented moles, some of which already showed signs of irritation, and that there has not been the development of a single malignant tumor in this series; and this in spite of the assertions made by many surgeons and dermatologists that it is dangerous to excise a mole, and that it should always be removed with the cautery. As already stated, every pigmented mole that appears late in life, as well as every pigmented mole that begins to grow or that shows any sign of irritation, should be removed at once; in fact, every pigmented mole that is liable to chronic irritation should be eliminated. The large more or less pigmented nevi occasionally become malignant, giving rise to either sarcomas or carcinomas. The small ones, if excised, never give rise to malignant trouble, but in the mind of the author it is doubtful if the large ones should be touched except for cosmetic reasons. There is no way of removing these large growths and having the wound heal by first intention; they can be removed only by electrolysis, cauterization, or some similar method, and in these cases malignant change is just as apt to develop upon the scar as in the old growth.

Vascular nevi rarely become malignant, but when they do they give rise to a virulent type of sarcoma. Still, it is doubtful, for the reasons stated in the preceding paragraph, if it is wise to remove them in order to prevent such malignant change taking place.

The various types of benign warts, commonly but erroneously called papillomata, only exceptionally undergo malignant degeneration, but every one that is exposed to trauma should be excised.

[2] Bloodgood: Amer. Jour. Med. Sc., 1914, cxlvii, 76.

Benign Tumors.—The various benign tumors become malignant much oftener than is commonly supposed. Bloodgood states that in the Johns Hopkins clinic there have been 406 cases of benign connective tissue tumors operated upon and 125 cases of sarcoma, a high percentage of which had their origin in the supposedly benign growths. With the single exception of lipomata, which never become malignant, and of keloids, which practically always remain benign, the probabilities are that from 5 to 10 percent of all other subcutaneous tumors become malignant if they remain undisturbed. Bloodgood has seen three cancers developing from simple wens. In nine of his cases of sarcoma there was the distinct history of a pre-existing fibroid tumor, and only sixty-seven instances of benign fibroid tumors. Hence he deduces that in about 13 percent of the cases a fibroid becomes malignant. Bloodgood's article should be read in the original by every physician.

Wounds.—Inasmuch as malignant neoplasms practically never arise in wounds that have healed by first intention, we should endeavor to cure all of the inflammatory conditions of the skin without leaving any scars. Lupus vulgaris should never be allowed to drag on, but should have drastic treatment when first seen. Old fistulas and ulcers should never be allowed to remain unhealed, for, while they do not frequently become the site of cancers, still each is in reality a potential cancer and should be so treated.

Arsenic.—Also, we should be extremely careful about prescribing arsenic in large doses over long periods of time, for, as already shown, this may result in the comparatively well-known arsenical keratoses that can become malignant just as other keratoses so often do.

Keratoses.—Keratoses are undoubtedly the precancerous dermatoses *par excellence,* and, once they have become established, should be thoroughly removed. This can be done by excision, or by the curette and caustic. The ordinary senile wart must never be regarded as harmless, for over 5 percent of them certainly develop into basal-celled cancers.

Education.—In addition to a search for the cause of cancer and the attempt to prevent the development of precancerous conditions, and the removal of them, once they have arisen, a number of other things are necessary if we are to make headway against this disease. We must educate the public to seek advice early, and we must educate the family physician to give good and wise counsel when this advice is sought.

Thanks to the medical profession and a few public-spirited publications, the public is becoming more and more awakened to the danger of cancer and the good results that can be obtained when the condition is recognized at a sufficiently early period, and every surgeon is noting that he is seeing not only more and more of early cancer, but more and more cases of the precancerous conditions. To again quote Bloodgood: "It is interesting to note that the number of these benign lesions applying for treatment is on the increase. Up until 1910 the percentage of these was but 14, in the past two years the benign precancerous lesions have increased to 30 percent, and the relative number of fully developed cancers is apparently on the decrease. . . . My table shows that between the years 1890 and 1913, sixteen patients have sought advice with lesions of less than a month's duration. (Practically all of these were recent cases, and in people who have been reached directly by the education of the students of the third and fourth year.) Fifty patients sought advice within two months after the onset of the first lesion; 77 between three and six months; 109 between six and twelve months; 344 from one to ten years or more." In the vast majority of instances, however, malignant change had been present upward of six months before operation was performed. In speaking of eight cases of perithelial angiosarcoma of the skin, Bloodgood says: "In five of these cases the tumor had been present one or more years; in only three cases less than a year. In every instance, therefore, there had been the opportunity for an earlier complete local operation. Not one of these eight cases was cured. If we are to get better results in dealing with the malignant tumors of the skin, we must see and treat our patients at an earlier date. The public must be taught to realize that nothing can be gained by delay. They should further be taught the danger of consulting men who are ignorant and mercenary, and absolutely without conscience. Every physician should have at hand a few copies of the American Medical Association's expose of those engaged in this nefarious trade.

There are, of course, a number of ways in which the public can be reached in such matters, but in my judgment none is so effective as the personal plea of the physician to a patient or household that has confidence in him. Public lectures, and articles contributed to the daily papers or to the public magazines have but a transient effect, and are usually speedily forgotten. And just for this reason it is necessary that every qualified physician and every embryonic physician shall have impressed on him the danger of precancerous affections, and should be taught not only in his course in pathology,

but also in surgery, medicine, and dermatology, the fact that a cancer nearly always arises upon the site of an abnormality, be it congenital or acquired. And in many medical schools this is not sufficiently well done. It is unjust to blame the busy practitioner for neglecting to keep up with these advances when he did not receive the proper instruction, but fortunately the ethical medical journals of today are teaching this very point, and emphasizing the necessity of recognizing cancer early. If the physician is in doubt, there is always an expert within call, a man who has the necessary ability and apparatus to make a diagnosis.

CHAPTER XVIII.

TREATMENT.

In dealing with the treatment of skin cancers, the following outline will be followed:

Surgical.
- Knife.
- Actual or electric cautery.
- Curette, with or without the use of a caustic.

Electrical.
- Electrolysis.
- Fulguration.

Actinic.
- X-rays.
- Radium.

Caustic.
- Nitric acid.
- Sulphuric acid.
- Acid nitrate of mercury.
- Chromic acid.
- Pyrogallic acid.
- Caustic potash.
- Arsenic.
- Silver nitrate.
- Zinc chloride.

Congelation.
- Liquid air.
- Carbon dioxide snow.

Medication.
- Arsenic.
- Methylene blue.
- Colloidal copper salts.
- Cancer vaccine.
- Immune sera.
- Supportative treatment.
- Analgesics.

Treatment of complications.
- Infection.
- Hemorrhage.
- Invasion of special organs.

Repair of deformities.
- Plastic operations.
- Artificial organs.

Treatment of inoperable cases.

SURGICAL.

Knife.—At times it is difficult to decide which is the best form of treatment for a special case. The patient usually dreads the knife, and likewise dreads an extensive operation for a small growth, and the physician must first gain the confidence of such a patient, and then point out the dangers incurred by doing an incomplete operation. But, in addition to the personality of the patient, the personality of the neoplasm must also be considered, and this the writer has endeavored to do in the chapters devoted to the special varieties of tumors. The author feels that excision with the knife is usually the preferable way in which to treat a tumor, for in this way a clean operation can be done with very little scarring, and it is possible to obtain a section of the tumor for microscopic study. This last should always be done, for in no other way have we a check as to what we are doing. The treatment of cancer without microscopical study is about as satisfactory as trying to read without eyes. This is because epithelial tumors vary markedly in their malignancy according to the type of cell from which they spring, and it is not always possible to make a diagnosis from a naked eye appearance alone, at least not until it has been many times confirmed by the histological study of similar conditions. Next to the use of the x-ray, the knife is the least painful of all modes of attack. And lastly, the results are the best, so far as one can judge by the study of statistics. So far as the writer knows, no dermatologist has kept an accurate list of statistics of the cases of cancer that he has treated by the curette or the caustic, and but few have checked up their x-ray results. So at the present time we can say that, so far as statistics go, the results with the knife are infinitely superior to the results obtained in any other way. Furthermore, in all surgical clinics it is noted that nearly one-half of all patients who apply for treatment because of skin cancer give the history of having been treated by a caustic paste, or by the curette, and often by the x-ray

or radium. At the same time, it is difficult to use the knife upon tumors that are situated upon the nose, eyelids or ears, and here some other form of treatment must usually be devised. In the cases of the prickle-celled cancers the knife is the only proper instrument, and this probably applies to the cuboidal-celled neoplasms as well. Sarcomata, endotheliomata, and the tumors arising from the glands of the skin should be treated by no other method.

Anesthesia.—Having once decided that the lesion is to be excised, the form of anesthesia must next be determined. In the smaller tumors it is usually possible to operate under local anesthesia, and for this purpose there is no better substance than the well-known Schleich's solution, made without the addition of morphine. Schleich's solution is essentially a one-tenth of one percent solution of cocaine in normal salt solution. There is not the slightest necessity for using a stronger solution of cocaine, providing that the surgeon properly infiltrates the tissues. In fact, the use of more than one-third of a grain of cocaine at one sitting may be dangerous,[1] the patient showing either excitement or depression. It is very convenient to add a few drops of a 1 to 1,000 adrenalin solution to the cocaine mixture, for this will markedly lessen the amount of the bleeding. A fine needle should always be used, so that the solution will not escape through the needle track. The needle is inserted at a slight distance from the growth, usually about half an inch, and superficially just beneath the skin, so that the infiltration can be noted; if the injection be made deep into the corium, satisfactory infiltration will not ensue. It should always be remembered that it is very difficult to infiltrate scar tissue, and at times impossible, so cases showing much scarring are not suitable for local anesthesia. The injection of the anesthetic mixture must be kept up, through several punctures, until not only the tissue in and beneath the tumor is thoroughly infiltrated, but also an area at least one-half an inch beyond its margins. Anesthesia will be complete at the end of two minutes, if not earlier. Before using a local anesthetic, it is well to make one or two little scratches of the skin to indicate the intended line of incision, for when the growth and surrounding tissues are filled with fluid the original boundaries are often lost.

In extensive cases it is usually necessary to employ general anesthesia, and in growths around the mouth or nose there is great need for an expert anesthetist. Ether is usually employed for long operations, while nitrous oxide and oxygen may suffice for a short one.

Disinfection.—In the majority of cases it is best to disinfect the

[1] Cushny: Pharmocology and Therapeutics, New York, 1911, 313.

skin with iodine about ten minutes before beginning the operation, remembering that the iodine must always be applied to a thoroughly dry surface in order to be efficient.

Operation.—It is usual to take out an elliptical-shaped piece of tissue, the line of incision extending never less than one-fourth and preferably one-half inch beyond the margins of the growth if it be small, and several inches beyond if it be large or rapidly spreading. The direction of the long axis of the incision must be carefully determined, so as to put as little tension as possible upon the healing scar, and also so as to make the line of the healed scar coincide as nearly as possible with the normal lines of the skin. Upon the face the axis of the oval incision should also run in the same direction as the lines of the face in that particular spot or region.

It is unnecessary to say that only a very sharp knife should be employed, and that the knife should never touch the cancerous tissue proper, for fear of implanting some of the cancer cells upon the edges of the wound. If any of the instruments touch the diseased tissue, they must be immediately discarded and fresh ones employed. The incision should be made with as few strokes as possible, usually in small growths one to each side will suffice, although it may be necessary to make one or two more in the depths of the wound in order to entirely free the excised mass of tissue, which should at once be removed and laid aside. After the bleeding has been checked, the surgeon should examine the growth with his naked eye, but should not handle it. An assistant should section it and hold it for the operator in order that he may run no risk of contaminating his hands. The tissue should then be preserved for microscopical examination.

Closing the Wound.—The question of the closing of the wound is a serious one. The writer has noticed that when a basal-celled cancer recurred, this recurrence almost invariably took place at the edge of the scar and not in the depths of the wound. This means one of two things—either that the incision was not wide enough or that implantation took place on the edge. In practically all of his more recent operations he has cauterized the edges of the cut with either pure carbolic acid or with the acid nitrate of mercury, and since that time has had very much better results, although the appearance of the scar has not been nearly so good. If it be determined to close the wound by first intention, silk sutures are usually used, and a sufficient number employed to accurately approximate the edges throughout their entire length. This is especially necessary if there be much tension. The needle should be sufficiently

strong, for at times the skin is remarkably thick and leathery, and prone to break needles unless they are carefully handled. The stitches should usually be removed on the second day, although in cases of tension this may not be possible. At first the wound may be dressed with silver foil, over which a piece of sterile gauze is placed, and sealed with either collodion or adhesive. Or the wound may be painted with iodine, smeared with a little sterile ointment to prevent the adhesion of the gauze that is placed next to it. After the stitches have been removed, a little more iodine may be added, and the wound dressed with cotton and collodion. In the case of a small growth the wound should be entirely healed by the end of the tenth day, although it is well to leave collodion on for a few days longer in order to remove strain and prevent the possibility of the edges separating.

Actual or Electric Cautery.—For many years some surgeons have felt that, when they employed the actual cautery rather than the knife, there was less danger of cancer recurrence in the edges of the scar. Halsted, as well as many others, has noted this in cancer of the breast. Were it not that the electric cautery is liable to get out of order in the ordinary operating room, it would be the ideal one, but, as it is, the actual cautery is the more reliable. Excision can be managed by the cautery as well as by the knife, although in the removed tissue it is impossible to determine the limits of the neoplasm. As a consequence, some surgeons prefer to excise with the knife and then immediately employ the cautery. It is generally considered somewhat dangerous to employ the actual cautery in the presence of ether fumes. The cautery has the one great advantage over the knife of thoroughly searing the edges of the wound, so that no cancer cells can escape into the vessels or become implanted along the line of incision. In extensive cases of cancer upon the limbs or body the cautery is excellent, although it cannot, for example, be used near the eye. The cautery should always be used when it is not possible to give a wide margin, as in lesions of the tongue.

Curette, With or Without Use of a Caustic.—The use of the curette without following it by a caustic of some kind is mentioned only to be condemned. An occasional case may be cured by the vigorous use of this instrument, but a brief recollection of the pathology of a cancer will show that it cannot reach the cells that are progressing into the still healthy tissue.

If a wound is, however, thoroughly curetted and then efficiently cauterized, the results are often excellent. Sherwell[2] has elaborated

[2] Sherwell: Jour. Cutan. Dis., 1910, xxviii, 487.

a method in which he employs the acid nitrate of mercury as the cauterizing agent, and has had excellent results. Other dermatologists, including the author,[3] have likewise obtained good results from its employment. The following account is taken from the writer's own article on the subject.

The acid nitrate of mercury, or the liquor hydrargyri nitratis of the Pharmacopœia, is made by dissolving 40 grams of the red oxide of mercury in 45 grams chemically pure nitric acid and 15 grams of distilled water.

The method is applicable to basal-celled cancers, endothelioma, moles, warts, and certain chronic infections, such as lupus vulgaris. Growths of the eyelid can be treated with very good results. It is possible to benefit, if not cure, rodent ulcers of very considerable size. In my judgment this method should not be employed in spino-celled cancers, as this variety of growth usually metastasizes rapidly.

Either local or general anesthesia may be employed. In small superficial growths thorough infiltration with a Schleich's solution will amply suffice. If the growth to be removed be about the face, it is better to give a preliminary injection of morphine and atropine, so as to lessen the secretions.

The apparatus needed is simple. Two or three curettes of various sizes (at least one of which must be sharp), a scalpel in case hard fibrous tissue is encountered, forceps, clamps, and especially a good actual cautery with which to stop bleeding, comprise the instruments. Four glass vessels should be provided, in one of which the acid nitrate is placed, another contains powdered bicarbonate of soda, the third a solution of sodium bicarbonate, and the fourth a 1 to 1,000 solution of adrenalin. In operations around the face the solution of the soda is essential for the protection of the eyes, or of the mouth or nose. In addition, there should be plenty of cotton swabs.

The operation is straight forward. Once the patient is anesthetized, all diseased tissue is rapidly and thoroughly curetted away, the small curette being necessary to reach into the various ramifications of the growth. The sense of touch will tell when one is dealing with sound or diseased tissue. All diseased tissue must be removed; one must not consider what the scar will look like, for the permanent removal of a malignant growth is far more important than speculation as to the cosmetic result. Curettage being completed, the bleeding is stopped by pressure, by the use of the adrenalin, or by the actual cautery, or, if necessary with clamps. Af-

[3] Hazen: Washington Med. Annals, 1912, xi, 246.

ter the field is entirely dry, the acid is applied with a cotton swab; this is allowed to act for from fifteen to twenty minutes, several applications being made. Dr. Sherwell considers that the acid has a specific action upon cancer cells, but it seems to the author that it is simply a powerful and deeply acting caustic, which may readily be controlled. The dry soda is then applied with a gauze sponge until it has formed a crust over the entire area cauterized. In cases of congenital moles it is first necessary to blister the skin with carbon dioxide snow or with cantharides, and then apply the acid, neutralizing as has been described.

The after-treatment consists in keeping the lesion dry; the thick black crust that forms after neutralization is a sufficient protection for the wound. Dr. Sherwell considers that in epithelioma, and more especially in sarcoma, it is wise to administer Fowler's solution, alternating with Donovan's solution, for several months. There is always considerable edema and inflammation following the operation, but this needs no treatment, and is undoubtedly a good thing, as the inflammation may suffice to kill cancer cells that may have escaped.

The results, both immediate and permanent, are excellent. The scar is soft and white, and to be approached only by the x-ray scar; in the author's hands the scar resulting from the deep application of the carbon dioxide has been more noticeable. Sherwell reports that he has had about 10 percent of recurrences, most of which have been cured by a second operation.

Of course, other caustics may be used after the growth has been curetted away; one may use silver nitrate, taking care to obtain the pure silver nitrate, and not the ordinary lunar caustic stick. Some men prefer to apply a caustic paste and allow it to act for several hours or days, as the case may be, but the author prefers the immediate cauterization as being less painful and more efficient.

An operation of this kind is especially useful in the basal-celled growths that originate upon the nose, or in the naso-facial groove, upon the eyelids or upon the ears. A modification of the operation that has yielded excellent results in the hands of the author, at least in early cases, is the excision of the growth and the thorough cauterization with the acid nitrate. This has the advantage of giving a specimen that is suitable for microscopic study, and the scar is surprisingly good. Even in very extensive cases it is sometimes possible to hold the disease in check for a number of years and render the patient much more comfortable, and occasionally a cure may result in an apparently hopeless case. Sherwell reports a number

of cures in instances where the orbit is invaded, although the eye is, of course, lost.

ELECTRICAL.

Electrolysis.—By some the electric needle is used in one of two ways—either the entire lesion is removed by it, or numerous punctures are made into it, so that the body of the growth is destroyed. While this method will undoubtedly cure a number of cases of the early basal-celled neoplasms, it has never appealed to the author, because it affords no chance for histological examination of the growth, and because one cannot be certain that he has gone beyond the margins of the growth. It would seem to be applicable only in extremely old and decrepit persons who cannot stand a more severe operation. An ordinary sixteen-cell silver chloride battery can be used, connecting the negative pole to the needle. If the operator is willing to take time, there is no necessity of causing any pain to the patient, for just as good results can be obtained from the prolonged action of a mild current as from the rapid action of a strong one.

Fulguration.—Of late years the so-called fulguration has come into some prominence, thanks largely to the work of de Keating-Hart. Both the method of application and the results vary to some extent with the skill of the operator. Bainbridge[4] has recently written a concise review of the subject, and the following is derived largely from his paper.

The method known as *altofrequent cytolosis, altofrequent scintillation, effleuvation,* etc., was first employed by Riviere, of Paris, and was described by him in 1900. He advocated removing the tumor by surgical means and then applying high frequency sparks. A monopolar or bipolar current, with a short spark, of high frequency, high tension, and low amperage, is employed. Or a special apparatus using a monopolar current with a long spark may be used.

Oscillatory desiccation (Clark) consists in the production and sustaining of heat to cause the dehydration of the tissues treated. This is accomplished by a specialized, oscillatory high frequency current, delivered from a fine metal point and then through the air to the tissue.

Thermopenetration was first described by de Arsonval in 1896. It depends on the power of the high frequency current to cause a decided rise in temperature in tissues interposed between two electrodes. De Keating-Hart has used this method to render the tissues

[4] Bainbridge: Internat. Clinics, 23d ser., iii, 268.

more radiosensitive, and by Nagelschmidt and Doyen for the destruction of neoplasms.

Diathermy or *transthermy* was experimented with in 1907 by Nagelschmidt, of Berlin, von Brendt, Preeps, and Zeyneck, of Vienna, and de Kraft, of New York. The apparatus employed elevates the temperature of the deep tissues to any required extent, the tumor being destroyed by coagulation. The greater the amperage employed the greater the heating. The voltage employed is relatively low.

The term *bipolar voltaization* is applied by Doyen to the method in which the electrode of the apparatus is held away from the part under treatment, and the sparks allowed to play upon the area.

Fulguration (de Keating-Hart) is founded upon the premise that the monopolar long spark of high frequency and high tension acts not only upon the neoplasm, but upon the soil on which the neoplasm has developed. De Keating-Hart claims that the use of the high frequency short spark at a low tension acts as a tissue stimulant, but that a spark of the minimum length of 8 cm. applied for a sufficiently long space of time transforms a healthy area into a torpid wound, which heals largely by the contraction of the surrounding healthy tissue. It is considered that the same process that prevents the reformation of healthy epidermis after fulguration also retards or suppresses the growth of cancer cells.

As this method is the most important of the electrical ones before the medical profession today, it may be well to describe the apparatus used. The generating apparatus consists of a large coil and a rapid interrupter, which converts the street current of low voltage and high amperage into an interrupted current of high voltage and low amperage. The high frequency apparatus consists of an Oudin resonator, with spark gap and condensers of great capacity. The sterilizing and cooling apparatus comprises an air pump, driven by an electric motor, which forces air through an electric sterilizer, and the air is finally delivered at the electrode cool and sterile. The electrode consists of a metal mandril within a rubber tube.

The first step in the operation is purely surgical, consisting of the removal of the diseased tissue as completely as possible, then the spark is used for a long time, using sparks of high frequency and high tension, and applying them to the entire wound. The electrode should be kept in steady motion, and no carbonization of tissue should result. "Ten minutes of fulguration should be used on an area of ten square centimeters."

Bainbridge wisely concludes his article by stating that, although at the present time the results seem good, still it is too early to draw

any too optimistic conclusions, a statement with which all fair-minded men must agree.

ACTINIC.

X-rays.—In the employment of the x-rays for the treatment of cancer, three methods have been advocated; first, the treatment by fractional doses; second, the employment of three or four large doses; and last, the application of one or two maximum doses.

In this country the first named method has been the usual one.[5] A moderately hard tube is selected, and put at a distance of about four inches from the lesion. Exposures vary in time from ten to twenty minutes, and are given at intervals of two to four days, and continued until the lesion has disappeared, this sometimes requiring several months. It is necessary to produce a slight dermatitis, but not a severe burn. In many instances very excellent results have been obtained by it—results as good as those obtained in the later methods. As experienced and excellent an x-ray operator as Pusey still believes in it. At a recent symposium before the American Medical Association in the Section on Pharmacology and Therapeutics, Pusey[6] said: "I sympathize thoroughly with the scientific ideals which attempt to determine the limits of physiologic safety of Röntgen ray exposures, but up to the present time I have been constrained to hesitate to adopt the maximum dose method in my own practice. I have done this for three reasons. First, I am sure that I have had my best results by a technic that consists of fractional doses—not of a few heavy applications. Certainly in my own experience the attempt at a radical quick dose has not proved as therapeutically efficient as several cumulative doses. In the second place, I cannot get away from the feeling that we are running a considerable amount of danger in the use of massive doses. We can make all of the factors the same except one, and that is the factor of the individual, the personal equation of the patient. At any rate, I do not feel that one patient will react just as the next one will. If I can draw any conclusion from my experience, it is that there is a difference of susceptibility in patients. In the third place, to give a massive dose requires attention to a group of important factors, and I think that in routine work the danger of some error is not to be overlooked. As a matter of fact, I have been consulted today about a burn following a massive dose of Röntgen rays for destroy-

[5] Pusey: Principles and Practice of Dermatology, Phila., 1907.
Pusey and Caldwell: The Röntgen Rays in Therapeutics and Diagnosis, New York, 1904.

[6] Pusey: Jour. Amer. Med. Assn., 1913, lxi, 598.

ing ring worm, so that the idea of danger is not purely a theory. As for my technic, I give repeated doses of Röntgen rays until I produce my effect."

In such a method as this there are several necessities. The operator must thoroughly understand the capabilities of both his machine and tube; at first he must proceed carefully until he tests these instruments out upon each particular patient, and then he can give numerous sittings. The work is prolonged and necessarily rather expensive, and the patients often tire of it. Of course, it is absolutely essential that all of the surrounding skin be covered with lead foil, so that neither an acute burn nor atrophy and telangiectases can follow.

It was soon found that two exposures of twenty minutes each, using the same tube and the same amount of current, were just as effective as nine or ten exposures of five minutes each, provided that the former were not too long separated. These figures are, of course, merely given in round numbers—as illustrations and not as absolute facts. As a result, many men began treatment along these lines,[7] and in general the results were just as good as by the older method. There has been a marked shortening in the duration of the treatment, and not as much liability to atrophy and telangiectasis, but some danger of an acute burn. The use of the penetrometer to measure the quality of the rays and of the Sabouraud-Noire pastille to measure the quantity of the emanations has markedly lessened this danger, but it is still present, especially with the inexperienced operator.

The natural sequence of this treatment was to give one, or perhaps two, massive doses—doses measured accurately both as to quantity and quality. In America MacKee, of New York, has been the chief exponent of this idea, although, as he points out, the method is in common use abroad, and his results have been excellent (Figs. 69, 70). The following account is derived from his various papers on the subject, and from my own personal experience, which is identical with MacKee's.

MacKee and Remer[8] claim that an accurate measurement of the dose is as important in Röntgen ray therapy as in any field of medicine; that the massive dose, carefully measured, is both accurate and scientific; that the patient is spared the necessity of many visits to the physician's office; and last, that this form of treatment is bet-

[7] Lange: Jour. Amer. Med. Assn., 1913, lxi, 556.

[8] MacKee and Remer: New York Med. Jour., March 29, 1913. Amer. Jour. Röntgenology, Dec., 1913.

ter therapeutically. In explaining the last point, they say: "Several years ago it was customary to apply the x-ray to epithelioma in very small doses three times a week. It was not uncommon to hear of 30 to 150 or more treatments being given to one patient. Those who are familiar with past results will recollect that a certain percentage of the patients were permanently cured, while in an unfortunately large proportion recurrences were common. It will also be recalled that the recurrences were not only resistant to further x-ray treatment, but that in many instances the lesions failed to respond at all, and even became so malignant that they could not be controlled at all. There were instances, too, where the primary epithelioma underwent involution to a certain point, and, after remaining quiescent for a time, began to assume malignant tendencies while under the influence of the ray.

"As apparatus and technic improved so that the number of exposures in a given case was reduced, the unfavorable results and the recidives were correspondingly diminished numerically. In other words, the nearer the treatment had approached the massive dose method, the better have been the results. The application of small amounts of the x-ray to the skin for a long period of time will produce atrophy, telangiectasia, pigmentation with or without erythema, and, finally, epithelioma—i. e., a condition similar to xeroderma pigmentosum. It might be mentioned here that these features are far less likely to occur if a well-filtered ray is employed. They will develop, however, even with the filtered ray, if the applications are repeated often enough and are continued over a sufficiently long period of time. Is it not possible, therefore, that so much ray applied to an epithelioma might add to its malignancy?

"It has been proved absolutely that prolonged and excessive exposure to the x-ray can produce a cancer. It would seem advisable, therefore, in the treatment of epithelioma with the x-ray to give as nearly as possible the *exact* or *minimal* amount necessary to cure the individual case. This dose may be divided into *several strong* treatments, but not into *unlimited* and oft-repeated *mild* exposures."

MacKee and Remer admit that their results are no better than those of Pusey, who sticks to the fractional method of dosage, but they do claim that Pusey's results are far above the average because he is expert, and that their own results are much improved by the introduction of the newer method. Their technic, to quote their own words, is as follows:

"For the information of the reader who has had no personal experience with radiotherapy, it may be stated that there are the di-

rect and indirect methods of qualitative and quantitative measurements. The indirect method consists of judging the quality of the ray by certain fixed standards, the technic being closely associated with the personal equation, because hardly any two radiologists employ exactly the same type of apparatus. Briefly, the technic is as

Fig. 69.—Basal-cell epithelioma. Twelve years ago this patient had numerous ulcerating gummata, one of which was at the site of the present lesion. Antisyphilitic treatment healed all lesions excepting one upon the neck, which never at any time entirely healed. Ulcer has progressed considerably in past two years and has developed a very hard border. Histopathology is that of a deep-seated basal-cell epithelioma. (MacKee's collection.)

follows: A milliamperemeter is employed to ascertain the amount of current passing through the tube, the milliamperage employed being the same in every treatment. The anode of the x-ray tube

is always placed at a given number of inches from the skin. The parallel spark gap (or other instrument), which registers the resistance in the circuit, is adjusted at a certain distance. By working with these constants, having had a great deal of experience, being thoroughly acquainted with all parts of the various apparatus em-

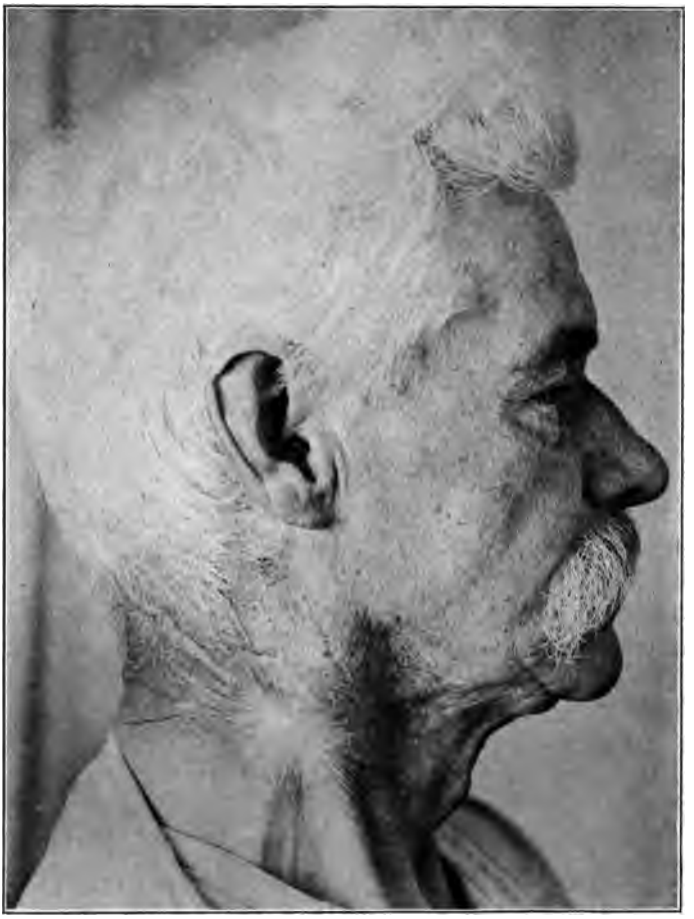

Fig. 70.—As a result of one massive dose of x-ray application, consisting of H 8, B 10, the lesion healed. Eight weeks later a second application of the same quantity and quality was administered as a prophylactic. A piece of the scar was removed for histological study and no evidence of malignancy could be detected. (MacKee's collection.)

ployed at the moment, and, above all, possessing a knowledge of all possible sources of error, one is enabled to estimate the penetration (quality) and the amount of ray administered. The accuracy of

this technic, while being sufficient for repeated small doses, does not possess the exacting requirements of the massive dose method. This view may have to be modified in the future, but, with the exciting apparatus and tubes available at present, we do not consider that our position is too skeptical.

"The direct method of measurement consists of utilizing many of the factors of the indirect technic, with the addition of employing instruments designed for the purpose of directly estimating the quality and quantity of the ray. There have been many types of apparatus and many schemes advanced with this object in view. There are, for instance, the Holzknecht chromoradiometer and radiometer, the Sabouraud-Noire radiometer, the Bordier chromoradiometer, the Bordier-Galimard units, the Guilleminot fluorometric quantiometer, the Kienböck photographic quantiometer, the Schwarz precipitation radiometer, the Hampson radiometer, and many devices and schemes originated by Freund, Schmidt, Haenisch, and others for the estimation of the quantity of the ray administered. Without going into detail, we believe that the Holzknecht radiometer (not the chromoradiometer), employed with a modified technic, is the best procedure to follow for the purpose. In our hands this technic has proved eminently satisfactory, and, although not theoretically accurate or 'fool proof,' the possibility of error, in the hands of the experienced operator, is reduced to the minimum.

"This idea of estimating the quantity of the ray is based on the change in color of a tablet of platinocyanide of barium which has been exposed to the x-ray. A standard color scale is utilized for comparison. The color changes are estimated in Holzknecht (H) units. The unit 1 H is one-third of that quantity of ray which can induce a mild erythema on the face in an adult. The dose varies with the age of the individual and the part of the body exposed. Skin that has been exposed to irritating chemicals will respond more quickly than normal skin. Fair skin is slightly more susceptible than dark skin. Beyond these variations it is a very rare thing to see an example of hypersusceptibility.

"Many instruments have also been designed for the purpose of judging the penetration or quality of the ray. Most notable are the Benoist radiochrometer, the Benoist-Walter, the Wehnelt, and the Walter scales. We have found the Benoist radiochromometer sufficiently satisfactory for this purpose."

In their work, MacKee and Remer have found it better to use a "hard" tube; in the superficial type of cancers they employ a B 8 tube, and in the deeper type they may use a B 10 tube—that is, a

tube that will measure 8 or 10 units by the Benoist scale when tested for penetration.

The technic for measuring quantity merits a somewhat fuller description, for it is not generally employed in this country. The Holzknecht radiometer consists of a suitably tinted celluloid band, the colors of which grade from zero to 8 H units. The measurement pieces consist of pastils of platinocyanide of barium, and the estimation is made by placing a half pastil under the colored band. Another half pastil is exposed to the emanations of the tube, while the patient is under treatment, covered with celluloid, and placed in contact with the "index" half pastil, but outside of the colored band. The whole pastil is now moved down the scale until the two halves match exactly in color, and a reading is then made, somewhat as on a hemoglobinometer.

As regards dosage, the Holzknecht units are now pretty generally known and used. As already stated, 1 unit equals a dose that is one-third large enough to produce erythema of the face in an adult. The H units are accurate only when a "medium" tube is employed —a B 6 tube, for instance. It is necessary to remember that 5 H with a hard tube may produce only a temporary alopecia, while the same dose with a soft tube may cause permanent baldness, and hence it can be seen that the biological effects of the H units vary according to the quality of the ray. As a general rule, from 5 to 7 H units are employed at the first sitting, and, if necessary, four weeks later another dose of about the same size given.

Regarding the "skin distance" and the "pastil distance," the authors say: "It is customary to place the pastil exactly half way between the anode and the skin. The reason for this is that the pastil, being closer to the anode, will assume a deeper color when in this position than when placed upon the skin, and, therefore, supposedly greater latitude is obtained in estimating the change in tint. Paradoxical as it may seem, the deep orange shades are harder to match than the paler colors. Not only are the green, yellow, and lighter orange tints easier to match, but they do not fade so rapidly when they are exposed to light and moisture. Contrary to what has been published, the color acquired by an exposed pastil will fade almost as rapidly under the influence of strong artificial light as by the action of daylight, and the deeper orange tints will attenuate far more rapidly than will the paler colors. These are some of the reasons why we prefer the full 'skin distance' for the pastil. There are, also, other very important reasons. The numerals on the scale of units of the Holzknecht instrument are not equally spaced.

. . . One has more latitude in comparing the lighter than in estimating the darker tints. . . . The pastil must be placed at least one inch from the wall of the tube to avoid the deleterious effect of heat, and hence the tube can be placed nearer the patient and the exposure shortened. . . . With the pastil on the skin, regardless of the distance of the anode, the H units must be multiplied by four to conform with the law of inverse proportions to the square of the distance—that is to say, if 1 H unit is administered in this manner, it will equal 4 H units by the 'half distance' method."

The fresh pastil is of a glazed brilliant green color, and all pastils should have this color, approximately at least. They should be kept in a well-ventilated humidor that is kept in a cool room. A used pastil can be returned to almost normal color by the action of daylight and moisture. Either the English, French, or German pastils may be used, for all seem about equally reliable. It is better to use fresh pastils each time.

Now a word as to the choice of method. Undoubtedly it is better in every particular to use as little x-ray as possible in the treatment of cutaneous affections, and this can best be done by a technic which approaches that just described. At any rate, we should make some attempt to measure our doses—this is just as important as to standardize the drugs that we administer by mouth. To the author it seems certain that in the next decade practically everyone will use instruments of precision in determining not only the quality, but the quantity of the rays that he uses. At the same time it must be remembered that very bad results are occasionally obtained when one attempts to use the massive dose. Most of these reports have come out of the dry states in the west, where there is a comparatively low humidity, and it seems possible that the lack of moisture may affect the sensitiveness of the pastils; at any rate, there have been a number of very bad burns reported. Also, it is more than possible that all skins do not act equally, and that what one skin will tolerate will prove very irritating to the next.

The results of x-ray therapy in cancer of the skin have usually been good in the hands of experienced men. Pusey[9] reports 72.5 percent of successful results in 111 unselected cases, comprising both the basal- and prickle-celled variety of cancer. Still later Pusey[10] admitted only two failures in thirty-five selected cases of cancer of the lower lip, mainly, however, of the rodent ulcer variety. MacKee's results have been almost uniformly good, and there can be

[9] Pusey: Jour. Amer. Med. Assn., 1907, xlix, 1215.
[10] Pusey: Jour. Cutan. Dis., 1913, xxxi, 73.

no doubt that the x-ray can accomplish cures in very many cases of cutaneous cancer, provided that no metastasis has taken place to the neighboring glands. The results are not, however, as sure as they are with the knife, for we find a certain percentage of cases that are absolutely intractable to the rays, the treatment is usually more prolonged, and, if a dermatitis be produced, the treatment is usually more painful. And, finally, in the hands of an expert surgeon there is not a great difference in the scarring produced by the removal of a small tumor. The x-ray has, however, a great field of usefulness. It is the ideal treatment for basal-celled cancers of the eyelids, of the naso-facial folds, and of the ears. In addition, it is useful in the very old, who cannot well submit to an operation, and in certain very extensive cases of cutaneous cancer. In some of these cases it will render the patient comfortable and prolong life, even if it will not cure. The general tendency is for the x-ray expert to belittle surgery and for the surgeon to make light of the rays, whereas in reality each field of therapy has a great field of usefulness.

Radium.—At the time of writing, radium[11] is receiving more than its share of notoriety, both in the daily press and before the various medical societies, as a cure for cutaneous cancer. In fact, radium seems to be going through the same stages that the x-ray has—first, it has created wild enthusiasm, then deep disgust, and finally it has found its true place. The general trend of opinion is that radium must be used in large quantities and the application must be for a considerable period—that is to say, the present tendency is to use it in "massive doses" just as in the case of the Röntgen rays.

While the greater portion of the radium in the world is produced in America, it has been used much more abroad than at home; in fact, the majority of American dermatologists have been profoundly skeptical concerning its value, and this is hardly to be wondered at when one considers the undue enthusiasm with which it has been advocated by certain men on both sides of the Atlantic ocean.

Radium is usually employed in the form of the bromide. Its general action seems to be comparable to that of the x-rays, but rather more powerful. It is known that three classes of rays are given

[11] Lawrence: Radium Therapy, Melbourne, 1911.
Wickham: Arch. f. Dermat. u. Syphil., 1912, cxi, 161.
Wickham et Degrais: Radiumtherapie, 2d ed., Paris, 1912.
Newcomet: Internat. Clinics, 23d ser., ii, 268.
Williams and Ellsworth: Jour. Amer. Med. Assn., 1913, lx, 1694.
Simpson: Jour. Amer. Med. Assn., 1913, lxi, 80.

off by it, and these rays are called the alpha (α), beta (β), and gamma (γ). The alpha rays possess but little power of penetration, and are somewhat deviable by a magnet. They can be absorbed by an air cushion of three inches thickness, by glass, or thin aluminum. The beta rays have much more penetrative power, but are more easily deviated by the magnet, and are said to coincide with the cathode rays of a Crookes' tube. Wickham thinks that they have curative properties of their own. The gamma rays penetrate deeply and do not respond to magnetic influence, and will easily pass through 2 mm. of lead. Radium also gives off an emanation that obeys the laws of gases, and that has become useful in the field of therapy.

When employed upon superficial cancers, all of the rays are usually employed, and no attempt is made to filter out the softest, which are presumably more irritating to the skin. Radium is usually kept in aluminum containers, or at least containers with aluminum windows, and these are brought in direct contact with the diseased tissue. As a general rule, an attempt is made to secure "cross-fire" action—that is to say, radium is applied to several sides of the growth at the same time, so that the rays will cross each other, and this is deemed much more effective than when applied at one point only. From 10 milligrams up are now applied at each point and left for from four to eight hours. It is, of course, essential to have radium that is very active, and many specimens are lacking in this respect, which fact undoubtedly explains the skepticism with which this remedy is viewed by many dermatologists and surgeons.

The rays of radium markedly resemble the x-rays in that they have an undoubtedly selective action for certain diseased cells, chief of which are the cancer cells. The author has seen instances in which an unsuspected focus in apparently healthy tissue was destroyed by the action of radium, leaving a tiny ulcer. The rays seem to kill the cancer cells, or at least to inhibit their growth, and not to inflame the normal tissue when carefully used. At the same time, it must be remembered that very serious burns can result from the use of radium, burns that are in every way comparable to x-ray burns, and hence the remedy must always be used with great care.

There can be no doubt that large quantities of radium, when used for a number of hours, can favorably influence the disappearance of cancer. There are probably only two styles of cancer of the skin in which it is justifiable to use it as a routine—the very early growths of the basal-celled variety that are situated where operation would be difficult and mutilating, and in inoperable growths. While a

number of men in America are at present claiming brilliant results, and while Wickham and Degrais have at times accomplished wonders, the attitude of the author is one of great skepticism, and for this there are the following reasons:

1. He, at the present time, has under his care three patients who have been treated with radium and pronounced cured, when in reality this was not true, in two instances at least the disease being made much worse.

2. The "cured" cases have not been followed for a sufficiently long space of time; it takes at least three years, in cancer of the skin, before one can regard a patient as definitely cured.

3. Because one cannot be absolutely certain as to the quality of the radium on the market.

As already pointed out, the only way to use radium is in "massive doses," and, inasmuch as the metal is extremely expensive—and inasmuch as at least $15,000 to $20,000 worth is necessary to even make a beginning, it is extremely improbable that this treatment can ever become very general. Personally, the author is very much inclined to agree with Bloodgood in his statement that radium as now used is holding back the correct therapy of cancer, and is a menace rather than an aid.

At the same time, it must be admitted that radium can do great good.

In conclusion, it must be stated that the last word has not been said regarding radium therapy. The author is inclined to believe that it is no better than a massive dose of x-ray, except in some few cases where the rays have failed, and even here radium is apt to prove useless. Its application is more convenient than that of the rays, but it is more difficult to gauge the dosage. We should keep an open mind on the subject at present.

Within the past year or two *mesothorium* has been used by some clinicians as a substitute for radium, as it is much less expensive. It seems, however, not to be as effective, although opinions as to the degree of difference still vary, but all observers are agreed that in the course of four or five years it entirely loses its radioactivity. The same statements would seem to apply to thorium-x and radiothorium, while the emanations from uranium are extremely feeble.

The proprietary remedy *thoremedin* has been carefully studied by Pusey,[12] who reports that its beneficial results were entirely due to the amount of sulphuric acid contained.

[12] Pusey: Jour. Amer. Med. Assn., 1912, lviii, 715.

Nitric Acid.—Nitric acid has been very little used as a caustic in cases of skin cancer, although it is greatly used in such horny growths as warts. This lack of use is rather surprising, when one considers that it is a deep-acting caustic, and that it can be speedily neutralized by an alkali. Possibly the reason is that the physicians fear the pain resulting from its application. At any rate, it is certain that the scar resulting from its use is not as good as that obtained from the action of many other caustics.

Sulphuric Acid.—Sulphuric acid[13] has practically the same action as nitric acid, but, as a general rule, does not act so deeply; it is practically never used.

Acid Nitrate of Mercury.—The acid nitrate of mercury has been especially extolled by Sherwell (see page 182), and his results with it have been excellent. Of course, he uses it by first curetting away as much as possible of the new growth, and then allowing the acid to act for at least fifteen minutes, finally neutralizing with bicarbonate of soda, as has largely been described. Its action seems to be much deeper than that of either acid described above.

Chromic Acid.—Chromic acid is but little used in dermatology, except in an attempt to destroy leukoplakia upon the tongue. The actual cautery can well replace this caustic.

Pyrogallic Acid.—Pyrogallol is considerably used by some men, largely because it is supposed to have a selective action and to spare healthy tissue, while destroying the cancer cells. It is usually employed in a 10 percent strength, but the author agrees with Stelwagon[14] that this is entirely too weak, and that, to expect any results, a 25 percent strength must be used. The following prescription would be about correct:

℞ Pyrogalloli ..... ℥ij
Vaselini,
Resinæ cerati, āā partes æqualis ad..... ℥j

This mixture is spread upon gauze and kept closely applied to the cancer, changing the dressing twice daily. At the end of five to eight days a slough will form, which will shortly separate, or which may be loosened by means of a poultice. The part is then cleansed, and the treatment continued until the physician thinks that sufficient tissue is destroyed. As a general rule, this method has one commendation—the lack of pain caused.

[13] Pusey: Jour. Amer. Med. Assn., 1913, lx, 434.
[14] Stelwagon: Diseases of the Skin, Phila., 1914.

CAUSTICS.

Caustic Potash.—Caustic potash[15] is a powerful caustic, and must be used with care, for it is extremely rapid in its action, and often this action is much deeper than was originally intended. The caustic stick should be employed rather than the solution, which may be accidentally dropped upon other parts than intended. Usually only one or two minutes' application is necessary, and the further action can be stopped by acetic acid or vinegar. The use of this caustic is extremely painful for the moment.

Arsenious Acid.—Arsenic, or rather arsenious acid, is undoubtedly the most popular caustic in the hands of the dermatologists. It is frequently employed in the form of Marsden's paste, which is made by using two parts of arsenious acid and one part of mucilage of acacia. Arsenic is supposed to have a selective action. It should never be applied to a surface more than one inch square because of the possibility of absorption and consequent poisoning. Either cocaine or orthoform is usually added to the paste to lessen the pain of application. It is usually allowed to act for from twelve to thirty-six hours, and a good deal of inflammation results. A slough results at the seat of application, which separates slowly. Many eminent dermatologists extol arsenic, Gottheil,[16] Marsden, Robinson,[17] Stelwagon, and others thinking very highly of it.

Silver Nitrate.—Silver nitrate is of value only after a thorough curetting, for its action is very superficial, owing to the formation of silver albuminate on the surface. Care should be taken to use only the pure molded silver nitrate, and not the ordinary lunar caustic, which is greatly inferior.

This caustic should not be used after cauterization; a more deeply-acting one should be selected. At times it may be used to stop oozing that results from the excision of a small neoplasm, but a touch with the actual cautery is much more efficacious. In reality this, as well as practically all other caustics, could be well dispensed with in cancer work.

Zinc Chloride.—Zinc chloride was formerly extensively employed by dermatologists, and still constitutes the basis of many quasi-cancer pastes. This salt is very painful in its action, and destroys healthy or diseased tissue indifferently. Its action is peculiar in that it seems to dry up the tissue rather than corrode it. It is most com-

[15] Van Harlingen: Jour. Cutan. Dis., 1906, xxiv, 345.
[16] Gottheil: Treatment of Skin Cancers, New York, 1899.
[17] Robinson: Internat. Jour. Surg., 1892, 179.
Internat. Jour. Surg., 1893, 164.
New York Med. Record, Mar. 31, 1900.

monly used in the form known as Bougard's paste, the formula for which is:

℞ Farinæ tritici (wheat flour),	
Pulveris amyli, āā	3ss
Pulveris arseni trioxidi	gr. iv
Pulveris hydrargyri sulphidi rubri,	
Pulveris ammonii chloridi, āā	gr. xx
Pulveris hydrargyri chloridi corrosivi	gr. ij
Zinci chloridi crystallisati	3iv
Aquæ fervidæ	3j

The first six ingredients are mixed separately and the zinc chloride dissolved in the water, and the two parts then rubbed up together. It takes one or two days for any amount of destruction to take place, usually one or two applications being necessary. This prescription should appeal to those who still believe in polypharmacy, the "shotgun artists."

Formalin is extolled by Ravogli,[18] who first curettes and then applies it in equal dilution with cresol and perchloride of iron. He reports excellent results, some of his cases having been followed for many years.

In general, the author is not favorably disposed to the use of caustic pastes, except after either curettage or excision of the growth, or in the case of extremely old or feeble individuals. There is no doubt that many of the small basal-celled neoplasms can be destroyed by the use of a caustic paste alone, but the mere fact that very many of the patients with cancer of the skin who have come to the Johns Hopkins Hospital surgical department for operation have had this method of treatment tried upon them is sufficient refutation of its universal efficiency. In these cases the report of the patients invariably was that the treatment was extremely painful, and that it left a large ulcer that was extremely difficult to heal. When these facts are explained to the patient, it is usually not difficult to secure his consent to an operation. In ten years' practice the author has not once had to resort to a caustic paste because the patient refused operation. As already pointed out, if a true selective action exists, which in many instances is doubtful, it makes the prognosis infinitely worse, because cancer cells are invariably found invading more or less deep down in the healthy tissue, the cancer cells existing in small groups. After operation, however, the use of a caustic upon the edges of the wound undoubtedly decreases the

[18] Ravogli: Amer. Jour. Surg., May, 1913.

percentage of recurrences, and has now become almost a routine in the practice of the author.

CONGELATION.

Liquid Air and Carbon Dioxide Snow.—Congelation has been used in two forms—first in the form of liquid air,[19] which was always difficult to obtain and more difficult to keep, and in the form of carbon dioxide snow, as advocated by Pusey.[20] The snow is best obtained by loosely screwing a small brass cylinder to the outlet valve of a commercial tube of the gas, which is supplied to all druggists for the purpose of charging their soda water, and then tightly tying a piece of chamois over the end of the tube. In this way a molded pencil of the snow is obtained ready for use. It is best handled in a pair of heavy, lined automobile gloves, and is applied to the growth for from one to three minutes, making firm pressure. The action is essentially caustic, and is not very deep. The author has seen it used in only four instances of cancer, and in all of them there was prompt recurrence; hence he does not advocate this form of treatment. Some other dermatologists, however, report successes from its use.

MEDICATION.

Arsenic.—Arsenic is still used internally by a few men, Sherwell, in particular, advocating it, and even Pusey seeming to think that it may have a slight inhibitive action. It is used either in the form of Fowler's solution or as Donovan's solution, the maximum dose usually being employed. There is no doubt of the value of this form of treatment in sarcoid and in the border line cases between sarcoid and sarcoma, but there is very little evidence that it is of any value in true cancer of the skin, other than acting as a general tonic.

Methylene Blue.—The internal use of methylene blue has been advocated by no less an authority than Jacobi[21] in internal cancer, that author believing that, while it will not cure the disease, it will at least hold it in check for some time. So far as the author knows, the internal administration of this drug has never been shown to have the slightest effect upon cutaneous cancer.

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[19] Dade: Trans. 6th Inter. Dermat. Con., 1907, ii, 672.
Whitehouse: Jour. Amer. Med. Assn., 1907, xlix, 371.

[20] Pusey: Jour. Amer. Med. Assn., 1907, xlix, 1354.
Jour. Cutan. Dis., 1909, xxvii, 32.
Jour. Cutan. Dis., 1910, xxviii, 352.
Low: Carbonic-acid Snow, New York, 1911.

[21] Jacobi: Jour. Amer. Med. Assn., 1906, xlvii, 1545.

Colloidal Copper Salts.—Within a short time preparations of colloidal copper have been injected into cancer patients. Loeb, McClurg, and Sweek[22] state that they "are now able to cause the gradual retrogression of human cancer, which until now has withstood various modes of treatment; and, furthermore, that the treatment does not seem to be limited to one kind of cancer, but applicable in the effective treatment of various kinds of cancer." Weil[23] has published a paper on the use of this method from the Cancer Research Service of the Cornell University Medical School, in which he details his experiments with and his clinical use of this method, and decides that this form of treatment is probably without value. Weil finds that the injections are not well borne, that they are followed by chills and rigors, and that nausea and vomiting are very common. In addition to these symptoms, there is usually a progressive anemia. Locally, there may result either phlebitis or periphlebitis.

Immune Sera.—The various attempts to produce either an active or a passive immunization against cancer is an extremely interesting one, but so far the results have been so contradictory that it would probably be a waste of time to attempt a description of even a few of them. The literature is voluminous, but speedily becomes obsolete.

A. E. Thayer,[24] of Mobile, has recently written a very interesting paper on epitheliolysis against cancer. He has worked on the assumption, now well grounded, that the injection of cells from one animal into the body of another would make the serum of the recipient animal lytic for such cells, and this was a specific reaction. In addition, the carcinoma cells are less resistant than normal epithelial cells; hence, if the lytic power of the serum could be raised, the cancer cells would be the first destroyed. In one case of inoperable cancer of the uterus, washed autolyosates of cancer were injected with apparently beneficial results. More confirmation is necessary before we can be sure of our ground.

At the Freedmen's Hospital we have tried to produce active immunization against epithelial cancer in a few cases. This was done by making an extract of a cancer of a similar histological origin, splitting it into toxic and non-toxic parts as suggested by Vaughan, and using injections of the non-toxic part once a week. The results were negative, although one patient did state that the injections were distinctly stimulating.

[22] Loeb, McClurg, and Sweek: Interstate Med. Jour., 1912, xix, 1015.
[23] Weil: Jour. Amer. Med. Assn., 1913, lxi, 1034.
[24] Thayer: South. Med. Jour., 1913, vi, 633.

Many attempts have been made to induce passive immunization by the injection of an immune serum. As Berkeley and Beebe[25] point out, this theoretically is an ideal treatment for cancer, for it is soluble in the blood, transmissible by the blood and lymph to all portions of the body, and should possess a selective affinity for the cancer cells. So far the very best results obtained with any of the methods proposed are simply mildly encouraging—no more.

Supportative Treatment.—In certain cases, either because of the advanced age of the patient, because of the extent of skin involvement or of the presence of a severe secondary infection, because of some other organic disease, or because of the presence of cancerous metastases, general supportative treatment becomes necessary. In certain of these cases it is questionable whether it would not be better to do a palliative operation, if only for the moral effect. But in these instances the patient, and not the disease, must be studied, and each victim furnishes a radically different problem, and one that must be solved according to the conscience and experience of the physician in charge, he usually being better able to determine in such a case than the consulting surgeon; this because of his supposedly better knowledge of the patient.

Supportative treatment, in general, consists of fresh air, good food, and the proper amount of rest or amusement, as the case may be. It is always essential to have an air of good cheer around such a patient, and a good nurse can sometimes accomplish wonders.

Analgesics.—So far as medicines go, about all that one can do is to employ simple tonics, or analgesics if necessary. Concerning analgesics, the author can see no good reason for withholding morphine from a patient who has an inoperable cancer; to him it seems needless cruelty. Of course, pain can often be relieved by dividing a nerve that is being pressed upon, or by some simple operation, but this is not always possible. As a general rule, it is probably advisable to start in with a combination of codeine, phenacetine, and aspirin, and not use morphine until absolutely necessary, for fear of it losing some of its effect when it has to be administered over a long space of time. It must likewise be remembered that either the x-ray or radium may greatly relieve pain, even though they do not cure the tumor. Dressing the new growth with charcoal, or with some mild antiseptic agent, may be a great comfort. An ointment composed of one dram of orthoform to an ounce of any fatty base will frequently relieve pain from exposed nerve endings.

[25] Berkeley and Beebe: Med. Record, 1912, lxxxi, 513.

TREATMENT OF COMPLICATIONS.

Infections.—When an epithelioma has been in an ulcerative condition for any length of time, it is not unusual for it to become infected, and this infection may be with a simple pyogenic organism, as the staphylococcus, or with some such germ as the proteus. In the putrefactive cases the odor is often horrible. In the former case, extension may take place and death result from meningitis. The first essential in dealing with an infection is to determine the character of the offending organism and the depth of the infection. In many cases the use of antiseptic wet dressing, taking care to use but little, so that there can be no poisoning from absorption, will relieve the trouble for the time being. In other cases it may become necessary to curette and cauterize, or to attempt an even more radical operation. In still other cases the uses of the proper vaccine, preferably autogenous, will greatly aid.

Hemorrhage.—In the case of hemorrhage it is sometimes difficult to decide just what course to pursue, and the decision must be made quickly. The hemorrhage can often be temporarily stopped by pressure, and sometimes permanently so, for there are usually proliferative changes in the wall of a blood vessel leading to an obliterating endarteritis, before erosion actually takes place. As a general rule, it is rather difficult to catch and tie the bleeding vessel, for frequently it is found that neither the clamps nor ligature will hold because of the diseased condition of the vessel that is doing the bleeding. In such cases it often becomes necessary to either put in a circular suture or to cut down upon the blood vessel that supplies the part and tie that. In the case of simple oozing, pressure or the cautery will usually suffice to check the condition.

Invasion of Special Organs.—When the invasion of the superficial or deep cancer becomes so great that other organs than the skin are involved, the problem of the correct treatment is always complicated. In some instances, as when the orbit is invaded, there is always danger of meningitis developing, and when the mouth is invaded the patient may starve to death. Treatment in all such cases must be according to the general lines of surgery and medicine—at least give the patient comfort, and relieve as far as possible all of the symptoms. Here each case must be decided on its own merits—no specific rules can be laid down.

TREATMENT OF INOPERABLE CASES.

The subject of the treatment of inoperable cases is not as painful a one as might appear, for much can frequently be done for them.

In the first place, many so-called inoperable cases are strictly operable if one has the courage to undertake the operation. Sherwell has thoroughly demonstrated this in some of his work. Of course, these extensive cancers look appalling to the novice, but to the expert there is often a great element of hope, especially if the tumor be of the basal-celled variety, and no metastases are to be feared. A thorough curettage, with excision of an area of skin around the edge, and then thorough cauterization, will often work wonders, and, even if it does not permanently cure, may make the patient comfortable for a number of years longer.

In the second place, radiologists have shown that many of the hopeless cases, even of a very malignant type, can be held in check or rendered comfortable for a long period of time. Radium will occasionally be beneficial even after the x-rays have lost their effectiveness, although this is not usually the case.

In other cases, proper dressing of the ulcerated areas and keeping them thoroughly clean will often accomplish brilliant results as far as the comfort of the patient is concerned.

In certain cases the blood vessels supplying the part can be obliterated and the growth of the tumor impeded from lack of nutriment.

And last, the patient can always be kept comfortable by the use of morphine if necessary.

REPAIR OF DEFORMITIES.

Plastic Surgery.—When a patient has been cured of extensive cancer of the skin, so far as concerns the removal of the disease, there is often much to be done to replace the deformity. Plastic surgery can do wonders. A new nose can be built up from a finger, new lips can be made from flaps from the cheeks, and many hideous deformities can be made much less noticeable by some similar means. This is not the proper place to dwell on such possibilities, for the subject is treated thoroughly in various text-books on operative surgery. It should, however, be pointed out that no plastic operation should be attempted until the cancer has been well for at least three years, as an operation may light up latent cells.

Artificial Organs.—If necessary, artificial parts can be supplied by various manufacturers. Artificial ears or noses can be procured, and, when properly tinted, to some extent are acceptable to the patient, although never as good as the manufacturers would have us believe.

In concluding this chapter, we must say that the time to treat a

cancer is in its early stage;[26] if it be of the nonmetastasizing type, complete local removal will suffice, but, if it be of the prickle-celled type, the neighboring lymph glands should be removed at the onset. The one object in the treatment of cancer is to wipe out every last cancer cell—not one must be left. To do this means the sacrifice of apparently healthy tissue, and the surgeon must school himself to do this, making the question of deformity an entirely secondary consideration. It is better to learn a few modes of treatment and practice them well rather than to have a superficial knowledge of all the varieties of attack; and, above all, tissue from each tumor should be submitted to competent histological examination, for in no other way can we increase our knowledge of the relationship between the pathology and the clinical course of the disease.

[26] Bloodgood: Jour. Amer. Med. Assn., 1910, lv, 1615.

CHAPTER XIX.

TUMORS ACCORDING TO LOCATION.

Hertzler,[1] in his admirable book on tumors, deals with neoplasms according to their location, and for further details the reader is referred to his volume. Many of the epithelial tumors, however, vary in malignancy, and hence in their clinical course, according to the region of the skin from which they arise. Also, it is impossible to treat tumors of different localities in the same way; for instance, one cannot treat a basal-celled cancer of the eyelid as he would a similar tumor upon the back.

Scalp.—The commonest new growths upon the scalp are of a benign variety; wens or warts are especially common. Malignant melanotic growths at times have their origin here. Cancer of the scalp is rather uncommon. According to Hertzler, von Bergmann found that out of 675 skin cancers in his clinic, 36 had their origin in the scalp. These tumors may be either basal-celled or prickle-celled, but the latter are probably the more common. Bloodgood states that out of 17 epithelial tumors, only 6 were basal-celled, and 2 of my own 3 cases were prickle-celled in character. In small basal-celled tumors, excision is the proper course, but in large neoplasms it is justifiable to try x-ray, because a plastic operation to repair the defect caused by extensive excision is very difficult. In the prickle-celled growths, broad local excision and removal of the neighboring glands is the best. Of course, in this location block dissection is impossible.

From time to time cases of malignant turban tumors have been reported. While these were given various names, and while the pathological examinations differed somewhat, still all of these growths had many clinical characteristics in common, and the name "endothelioma capitis" has been pretty generally applied. Ancell[2] recorded a case occurring in a 26-year old woman, and which was present for ten years. At autopsy metastases were found in the liver. Four relatives were similarly affected, but the disease remained local in all of them. Baker[3] reported another case in a man aged 24. Tumors developed shortly after traumatism, some of them

[1] Hertzler: Treatise on Tumors, New York, 1912.
[2] Ancell: Quoted by Hoffmann and Friboes.
[3] Baker: Quoted by Crocker, Diseases of the Skin.

underwent spontaneous involution, but one grew until it reached a diameter of 10 inches, when it was surgically removed and reported by the pathologist to be a fibrosarcoma. Cohn[4] reported an instance in a woman aged 52, who had the malady for twenty-six years. One of her children had the same trouble. The pathological diagnosis was "alveolar sarcoma of Billroth." Kaposi[5] reported a case in a man aged 60, who had been affected for forty years, and whose

Fig. 71.—Endothelioma capitis. (After Spiegler.)

daughter had a similar condition. Oro[6] saw a case which developed after injury, and which was thought to be a spindle-celled sarcoma. Barrett[7] saw the same condition in a mother and her two daughters. He called the growths "multiple sudoriperous adenomata." Spiegler[8] has carefully studied the condition and decided that the condi-

[4] Cohn: Jour. Cutan. and Genito-Urinary Dis., 1892, x, 393.
[5] Kaposi: Comptes Rendus de Cong. Internat., Rome, 1894, 135.
[6] Oro: Giono. Ital. d. mal. Ven. e. d. Pelle, 1896, Fass. ii.
[7] Barrett: Brit. Jour. Dermat., Feb. 6, 1892.
[8] Spiegler: Arch. f. Dermat. u. Syphil., 1899, l, 163.

tion was really endotheliomatous. Poncet[9] has described another case, calling it a cylindroma of the sebaceous glands. Haslund[10] reported a case in which metastases occurred. Hoffmann and Friboes[11] mention still other cases. Lawrence has seen the disease in a mother and daughter, and the pathological report was endothelioma.

Hoffmann and Friboes have described a case which they consider to be a perfect illustration of a benign basal-celled tumor. They are inclined to believe that the vast majority of these growths are basal-celled in character. Krompecher[12] agrees in this view. It is probable that various types of malignant growth can give a similar clinical picture, and that treatment must depend entirely on the microscopical findings.

Forehead and Temples.—Basal-celled neoplasms are not as common here as upon the face, but are fairly frequently seen. Sequeira,[13] in his series of 220 cases, saw nine upon the forehead and twelve upon the temples. In commenting on those of the forehead,

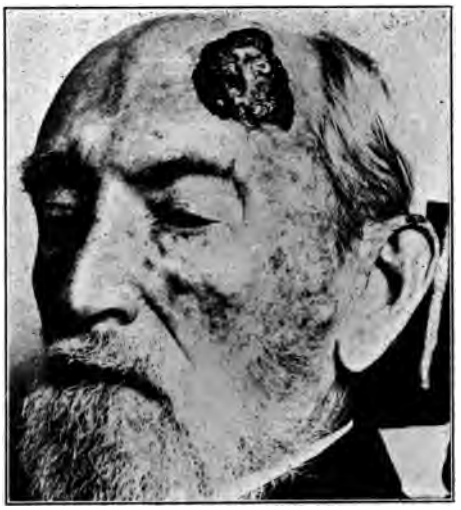

Fig. 72.—Basal-celled carcinoma of the forehead. (Heidingsfeld's collection.)

[9] Poncet: Quoted by Spiegler.

[10] Haslund: Quoted by Hoffmann and Friboes.

[11] Hoffmann and Friboes: Trans. 7th Inter. Con. Dermat. e. Syphil., Rome, 1912, 931.

Hoffmann: Deutsch. Med. Wchnschr., 1910, 2365.

Friboes: Beitr. z. Klin. u. Histopathol. der gutart. Hautepitheliome, Karger, Berlin, 1912.

[12] Krompecher: Der Basalzellenkrebs, Jena. 1903.

[13] Sequeira: Brit. Jour. Dermat., 1913, xxv, 172.

he says: "Here the ulcers are usually of the superficial cicatrizing type. They often start just above the root of the nose and extend upward in the frontal region." Crocker, in his specially illustrated book, has a very good cut of a case of this variety.

The tumors originating upon the temples seem to have a special tendency to become fungating. Basal-celled tumors arising in these localities are much commoner than the prickle-celled neoplasms (Fig. 72).

Eyelids.—Basal-celled growths are very prone to arise from the inner canthus of the eye, and to a slightly less extent from the outer canthus. Over thirty of Sequeira's cases had their origin in one of these locations. Tumors springing from other portions of the lids are comparatively infrequent, but nevertheless do occur, especially upon the lower lid. Bloodgood says that out of twenty-four epi-

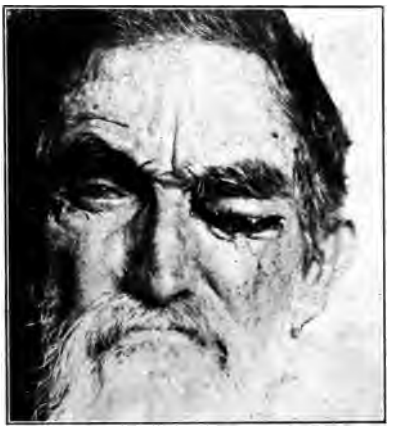

Fig. 73.—Basal-celled cancer of eyelid that has invaded the orbit. (Author's collection.)

thelial tumors, benign and malignant, originating upon the lids, twelve were of the basal cellular variety. Hence it can readily be seen that the vast majority of malignant tumors arising from the lids are not of the prickle-celled type. and therefore are not especially malignant (Fig. 73).

McDonagh[14] has recently written an interesting article on the pathology of the skin from the eyelids and naso-facial grooves, and concludes his article as follows:

"Tumors affecting the orbito-facial and naso-facial grooves are of epithelial origin, and atavistic of both the lower eyebrows and the

[14] McDonagh: Brit. Jour. Dermat., 1912, xxiv, 291.

specialized glands found in these regions in many of the mammalia. There is probably not an individual who will not show some trace of epithelial embryonic tissue (nevus) when a section is made from the skin of these grooves. All the tumors, from a simple hair-follicle growth to a rodent ulcer, are links in one chain, the former being the head or most mature, the latter the tail or most embryonic. As they are all links, the histological differences of one clinical entity are at once explained."

Clinically, these rodent ulcers usually spread rather slowly. As a general rule, the mucous membrane is spared for some little time, but eventually both it and the lachrymal sac are invaded and the

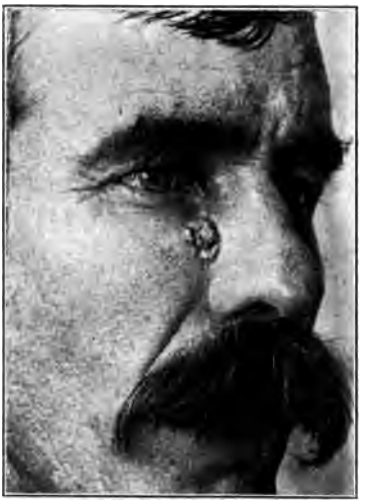

Fig. 74.—Basal-celled cancer of the nose; a common location. (Poole's collection.)

eyeball destroyed, while the socket becomes deeply involved. In a few instances the tumor may run lengthwise along the upper or lower lid. Sequeira states that tumors at the outer canthus usually spread downward and early involve the bone, but such has not been the experience of the author.

These growths are difficult to treat for two reasons—first, because it is difficult to satisfactorily repair a lid, and, secondly, because of the necessity of not injuring the eyeball. In the very early cases the writer usually either excises or curettes and then tries the x-ray. In later cases either the x-ray or an operation founded on that originated by Sherwell should be used. In late cases the Sherwell

operation[15] is undoubtedly the best. The majority of surgeons and dermatologists agree with these conclusions, even the most enthusiastic operators advising x-ray first. Caustic pastes must never be used, because of the proximity of the eye, and the inability to control their action.

Nose.—Tumors originating from the naso-facial grooves (Fig. 74) are almost invariably of the basal-celled type, and are commoner here than upon any other part of the body. Bloodgood[16] says: "The basal-celled tumor is situated most frequently upon the nose (50 percent, 13 out of 26 cases)." Tumors upon the bridge of the nose may be of any of the other types of cancer, and the prickle-celled variety the next most frequently encountered. It is usually a rule to consider that all tumors of the nose are rodent ulcers, but this is a mistake. A short time ago the author removed from the bridge of the nose a small tumor that had been present for over six months, and was surprised to find it to be a typical squamous-celled carcinoma. Fortunately tumors in this location grow slowly. Because of the difficulty of excising a growth in one of the grooves, it is better to use either the curette and caustic or to rely on the x-ray. In the spinocelled tumors it is impossible to do a block operation, so the glands must be left.

Ears.—Two distinct types of tumors arise from the ears—those having their origin upon the pinnæ, which are mostly rodent ulcers, and those arising from within the auditory canal, which grow very rapidly, being of the more malignant type. Heidingsfeld has had a very remarkable case where such a tumor arose from the mastoid region after an operation for an infection of this area. Tumors of the pinna are not often met; the author has seen only one, and Bloodgood reports only three. The rodent ulcer variety should be treated with either the röntgen rays or curette and caustic because of the deformity that must of necessity follow an operation with the knife alone. The deep tumors are probably hopeless from the start, but radical surgery might save a few.

Cheeks and Face.—Basal-celled tumors here are comparatively common. Bloodgood has seen fourteen out of a total of fifty-five cases of benign and malignant epithelial tumors. They usually arise about 2 cm. below the eyelids, but may occur elsewhere. Twenty-four of Sequeira's 220 cases had their origin upon the cheeks. When seen early, these tumors should be excised and the scar closed by a linear suture; or, even better, after excision the edges should be

[15] Sherwell: Jour. Cutan. Dis., 1910, xxviii, 487.
[16] Bloodgood: Progressive Medicine, Dec., 1904.

cauterized, and later a skin graft done. In extensive cases, either excision or a Sherwell operation may be performed, or the x-ray or radium tried.

Many of the neoplasms of the cheeks are of the malignant prickle-celled variety, and grow very rapidly. In such cases it is necessary to do a very radical operation, including the removal of the neighboring lymphatics.

Chin.—Basal-celled tumors of the chin are rare. Sequeira has seen only two such cases. Prickle-celled tumors are also rare. Bloodgood has had two instances of so-called basal-celled tumors where metastases took place to the submental glands, but is inclined to regard them as cuboidal-celled growths. Excision is the best treatment for growths in this locality.

Neck.—Considering the chronic irritation caused by collars, cancer of the neck is rare, although a few instances do occur. The neoplasms arising in this locality usually spring from moles, then forming nevocarcinomata, in the sense of Unna, or from congenital fibro-epithelial outgrowths, then forming typical rodent ulcers, more rarely squamous-celled neoplasms. Treatment is along the lines already indicated.

Lips.—Appreciating the earnest efforts of various authors and members of committees to educate the laity and impress on the profession the methods which should be adopted to improve results in the treatment of cancer, the author feels that he can best introduce the surgery of cancer of the lips by calling attention to certain facts which seem of special moment in cancer occurring in this situation.

Precancerous Lesions.—The surgical importance of any abnormality appearing at the mucocutaneous junction of the lips, especially the lower lip, at middle life or later, cannot be too much emphasized. If the lesion persists for a few weeks or over a month, although it may be only a slight scab (Figs. 75, 76), wart, induration, or little ulceration, it may be of the gravest significance, for this is exactly the way that cancer of the lip starts. There is always a precancerous stage, and this is the ideal time for interference. Bloodgood reports cases which show that a wart situated on the lower lip may become malignant within two months after its appearance. Cancer may develop in a pipe burn within two months, and a fully developed cancer with metastases to the glands of the neck is possible three months after the initial lesion is noted. The greatest risk is in the cases where there has been a delay of more than six months before operation. Hence these early persistent le-

sions should be excised with a margin of healthy tissue; generally a small wedge-shaped excision will suffice. This slight operation can be easily done under local anesthesia, and with little or no resulting disfigurement. The portion removed should be examined by a pathologist accustomed to differentiate epithelial growths. It is important not to curette, burn, freeze, x-ray, or treat with radium these early lesions because, should one have already taken on malignant changes, it could not be recognized until the patient returned with glandular involvement. When the latter are involved, the operation is a serious one, and the percentage of cures is very much lower than in the early cases. If the tissue prove, on microscopical exam-

Fig. 75.—This patient is suffering from a seborrheic keratosis of the lip. It would probably have become malignant had it not been removed. (Sutton's collection.)

ination, to be cancerous, the cervical lymph glands should be at once excised.

In early cases, before the lymph glands are involved, we can hope to cure about 95 percent of our cases, but after involvement of them has taken place the statistics show about 50 percent of cures. Our methods are improving, but two very vital factors in future success are early diagnosis and early operation.

Incidence.—Cancer of the lips is comparatively common in men and very rare in women, and usually occurs upon the lower lip. Steiner[17] reports 140 cases of cancer of the lower lip and 12 of the

[17] Steiner: Deut. Zeitschr. f. Chir., 1909, xcvii, 243.

upper, Judd[18] has had 153 of the lower and only three of the upper, while Rowntree[19] gives the ratio as 234 to 7, and also states that six times as many cancers are found upon the side of the lip as upon the center. Bloodgood's[20] statistics show 161 epithelial tumors of the lower lip and 21 of the upper lip. Cancer of the lip appears about or after middle life in the vast majority of instances (Fig. 77), but may occasionally develop in the young. Hertzler shows a marked example in a boy of 16, and the author illustrates a case in a man of 27 (Fig. 78). Cancer of the lip is much more common than benign affections of these organs.

Fig. 76.—This man has a very extensive seborrheic keratosis of the lower lip. (Sutton's collection.)

Etiology.—Irritation of the lips seems to be the most potent factor in the etiology. A smoker's burn of the lower lip is the commonest cause of irritation, but ragged teeth, or the habit of biting or picking the lips may cause sufficient irritation. Cigarette smoking, where the paper stuck to the lips and left irritation when removed, was apparently the cause of one cancer under the writer's observation. The early abnormality may be a slight ulcer or loss of epithelium, or there may be an epithelial hypertrophy and a re-

[18] Judd: Old Dominion Jour. Med. and Surg., 1908, vii, 399.
[19] Rowntree: Arch. Middlesex Hosp., 1908, vii, 119.
[20] Bloodgood: Jour. Amer. Med. Assn., 1910, lv, 1537, 1615. Surg. Gynec. and Obst., April, 1914, 404.

sulting wart. Some lesions may persist as benign lesions for several years, and then degenerate, but generally the change is early and often very rapid, as has already been stated.

Sarcomata.—In classifying the malignant tumors of the lips, mention must be made of sarcomata. Certain of the angiomata undergo malignant change, and must receive radical surgical treatment. More rarely, small round or spindle-celled sarcomata occur upon the lip. Markley[21] has recently reported such a case and collected several others from the literature. His patient was 65 years of age, and, because of this fact and because of the involvement of the cervi-

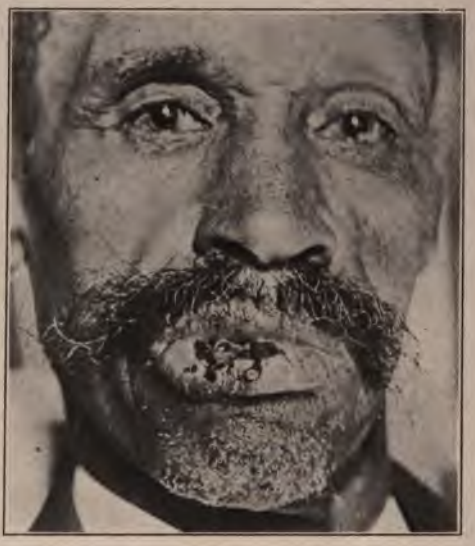

Fig. 77.—Ulcerated prickle-celled carcinoma of the lower lip in a negro, of two years' duration. (Author's collection.)

cal glands, diagnosis of carcinoma was made, but the microscope showed the lesion to consist of small round cells, a typical sarcoma As the tumor had been present for six months before radical operation was done, the prognosis was naturally bad. These tumors metastasize early, either through the blood stream or through the lymphatics, and operation must be done very early in order to save the patient.

Carcinomata.—The epithelial tumors of the lip are the most important for our consideration, for they are the common growths that demand surgical treatment. The lip cancers may be grouped under

[21] Markley: Jour. Amer. Med. Assn., 1913, lxi, 334.

two headings—the squamous- or prickle-celled type and the basal-celled variety. The malignant warts also deserve consideration, although they are practically always prickle-celled in origin. This classification is based on that of Krompecher. The cubocelled tumors are best included with the squamous-celled neoplasms, for they are of almost similar malignancy, and hence require the same treatment.

Basal-Celled Tumors.—Under the basal-celled type we may clinically have nodular lesions, usually beneath the skin, ulcers, fungi,

Fig. 78.—Prickle-celled carcinoma of the lower lip in a young man, which arose after treating a clinically benign lesion with caustic pastes. (Gilchrist's collection.)

or warts. The vast majority of the so-called rodent ulcers are basal-celled carcinomata, but occasionally a prickle-celled tumor may run a similar course, differing only in the fact that gland metastases result. Microscopically, the difference is easy to detect, as has already been sufficiently pointed out. Usually the clinical difficulty in diagnosis occurs only in the very early cases. The basal-celled growth has a greater tendency to appear as a subepidermal nodule, its growth is slow, and gradually a scab is formed; the latter comes away and an ulcer appears, or a fungous growth may develop.

Spinocellular Tumors.—The spinocellular cancer of the lip commonly starts at the mucocutaneous border, and the first symptom is

an area of induration, with slight ulceration. Both the induration and the ulceration tend to increase rapidly, and the submaxillary lymph glands soon become hard and shot-like. This growth often has the appearance of chancre, and the following are the chief diagnostic points. Chancre is common in the young; cancer is common in the old and rare in the young; cancer is very rare in women; chancre equally common in the two sexes; chancre is almost as common upon the upper lip as upon the lower, which is not true of cancer; in chancre the growth is much more rapid than in cancer, and the lymph glands enlarge much earlier; the spirochete can be demonstrated in chancre, and the histological pic-

Fig. 79.—Fungating carcinoma of the lower lip, of only five weeks' duration. (C. J. White's collection.)

ture of the two is radically different. A dose of salvarsan will cause the speedy disappearance of a chancre. It must always be remembered that a chancre will not give a positive Wassermann reaction—at least not until late in its course.

Metastases.—As already pointed out, the basal-celled growths do not metastasize to the lymph glands and are cured by a local operation. On the other hand, the commoner prickle-celled tumors speedily metastasize, and the presence of one demands not only local removal, but also removal of the glands of the neck because of the rich lymphatic drainage of the lips. Of course, it must not be overlooked that any ulcerating tumor of the lips may cause enlargement of the glands from simple inflammatory hyperplasia. In Blood-

good's statistics concerning malignant tumors of the lower lip, published in 1910, there were 100 spinocellular tumors, 2 cubocellular neoplasms (which we can include with the preceding), and only 4 basal-celled growths. In contrast, his figures concerning cancer of the upper lip showed 4 spino-celled growths and 9 basal-celled ones.

In determining the relative malignancy of a tumor of the lip, certain general rules hold as for epithelial tumors upon other portions of the body. Long duration, no history of any active growth,

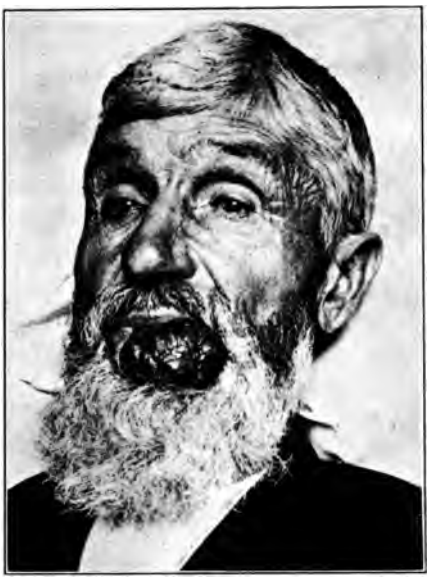

Fig. 80.—Fungating cancer of the lower lip of five years' duration. (Heidingsfeld's collection.)

absence of enlarged draining glands, tendency to remain pedunculated, a lack of definite induration at the base, all point in favor of a more benign type of growth.

Malignant Warts.—The malignant wart, already mentioned, is a prickle-celled tumor. Papillary epithelial tumors may be malignant from the onset, or may develop malignancy from a benign growth, but, as a rule, metastases from these tumors do not take place. Bloodgood[16] describes such a growth springing from the mucocutaneous border of the lower lip in a feeble old man, the tumor being of one year's duration. The tumor had a large papillary surface, which overhung normal skin, and was attached by a pedicle to the edge of the mucous membrane. There was no induration below

the pedicle. Because of the above facts the operator was able to conclude on operation, that the tumor was either benign or a very early papillary epithelioma. Local excision was performed, and early cancerous changes, limited to the wart, were found. Further operation was deemed unnecessary, and there was no recurrence. Bloodgood has observed seventeen malignant warts, and all but one has remained cured by operation, and in that case the local incision was not sufficiently broad. In nine cases merely a wedge-shaped piece was removed, and in eight the cervical glands were dissected out. In not a single instance did the glands show metastases. The dura-

Fig. 81.—Prickle-celled cancer of the lower lip of eight months' duration, lesion developing upon an old existing fissure. Patient refused operation upon glands of the neck and died eighteen months later as the result of metastases. (Heidingsfeld's collection.)

tion of the warts had been: in two cases, two months; in one case, five months; in the remaining cases more than six months, the longest ten years.

Treatment.—As has already been stated, excision of the growth with a good margin of healthy tissue and repair of the lip—in other words, the local operation—is a justifiable and harmless procedure, provided the glands are attacked at an early date should pathological findings make it necessary. Excision of a portion of the tumor or removal of a gland for diagnosis is quite another matter, and is

practically never justifiable unless performed on the operating table, where the diagnosis can be made either from the gross appearance of the tissue or from a frozen section, and both the patient and operator prepared to immediately go ahead with the complete operation should it be necessary. It has been definitely proven that, if a cancer is cut into and left, the chances of subsequent cure are very much diminished. When a cancer is incised for diagnostic purposes, certain precautions are necessary to prevent dissemination of cancer cells. The cut surface of the tumor should be treated with pure carbolic acid, iodine, caustics, or the actual cautery, drawn together and covered with gauze. All instruments used in connection with

Fig. 82.—Prickle-celled cancer of the lower lip of fifteen years' duration. Note resemblance to a rodent ulcer, but also enlarged glands beneath chin. Cured for four years by radical operation. This case illustrates the difficulty of diagnosing the difference between basal- and prickle-celled cancer of the lips. (Heidingsfeld's collection.)

the tumor should be boiled again, and towels and gloves changed before proceeding with the operation.

In advanced ulcerating cases of cancer it probably does no harm to remove a portion of the more superficial growth, if the vessels be seared with the actual cautery, but, in general, cutting into tumors for diagnostic purposes is to be strongly condemned.

Crile[22] emphasized an important fact when he stated that in a

[22] Crile: Jour. Amer. Med. Assn., 1906, xlvii, 1780.

careful study of 4,500 cases of cancer of the head and neck, exclusive of the thyroid gland, less than 1 percent showed secondary cancer in distant organs and tissues. Death in these cases nearly always results from the local or regional development of the disease. This means that "the collar of lymphatics of the neck forms an extraordinary barrier through which cancer rarely penetrates. Every portion of the barrier is surgically accessible."

According to Poirier, Cuneo et Delamere,[23] the lymphatics draining the lips are generally agreed to be the following. There is a small gland in the cheek situated well above the corner of the mouth, just above the fold of the cheek—one such gland on each side. Men-

Fig. 83.—Prickle-celled cancer of the upper lip. (Kerr and Hazen.—Courtesy of the Journal of Cutaneous Diseases.)

tion of this gland is not often found in the literature, but the author knows of two or three cases where it was personally demonstrated to be involved by cancer, secondary to cancer of the upper lip.

The submental group lies in a triangle bounded by the anterior bellies of the digastric muscles and hyoid bone; this receives vessels from the chin and central portion of the lower lip.

The submaxillary group, consisting of five or six, or even more, glands, lies in the submaxillary triangle, between the bellies of the

[23] Poirier, Cuneo et Delamere: The Lymphatics, 1904.

digastric muscles and the jaw, and drains the lower portion of the nose, the cheek, the upper lip, and the lateral portion of the lower lip. In the dissection of this group of glands the facial artery and vein should be ligated and divided, the submaxillary salivary gland should often be removed because of its close proximity to the lymphatic tissue, and Wharton's duct should be tied. Care should be taken not to injure the lingual and hypoglossal nerves, which cross the floor of this triangle. There is an anastomosis between the lymphatics which drain the two sides of the lip and also with those from the central portion, and hence any blocking of regular drainage, whether by cancer or inflammation, may cause the lymph stream to flow in any direction. As a result it is best to remove the glands upon both sides at the same sitting.

The deep cervical group of lymph glands (Fig. 84), estimated to comprise from fifteen to thirty glands, extends from the tip of the mastoid and posterior belly of the digastric muscle to the junction of the internal jugular and subclavian veins. Some of these glands lie in front, but a larger number lie behind the internal jugular vein. This is a very important group in surgery of the lip, because it forms the second glandular relay for the area which drains the submental and submaxillary glands. Consequently, when the submaxillary glands are involved, it is necessary that the entire deep cervical group be removed.

The author believes that the ideal treatment of cancer, in general, requires that the primary growth, along with the lymphatics draining the part, should be removed in one piece; there should be no division of lymphatics. It is not, however, necessary in most cases of cancer of the lower lip for the incision for the removal of the glands of the neck to be continuous with the incision in the lip. Witness the cases where the operation upon the lip has been done independently of that on the neck, and no appearance of cancer in the lymph vessels, which lie between the primary growth on the lip and the first relay of glands in the neck, has become manifest. Beckman,[24] in his report of these cases from the Mayo clinic, states that he has not observed a cancer occurring in the lymphatic vessels between the original growth and the lymphatics of the neck, and that cancer of the lip is either a local growth or a metastasis in the adjacent glands. Because of the danger of infection from the buccal cavity, it is of great importance that the local excision and the operation on the neck should be independent, and that the latter be done first, although both should be performed at the same sitting.

[24] Beckman: Jour. Oklahoma State Med. Assn., Oct., 1913.

In removing a section of lip which contains a basal-celled tumor or one of the malignant warts, or when the growth is small and recent, and there is a reasonable doubt that the lymphatics are involved, a local anesthetic is preferable to a general anesthetic. Cocaine (1 to 1,000) with adrenalin (1 to 10,000) in normal salt solu-

Fig. 84.—This illustration, redrawn after Crile, shows the relationship of the deep lymphatics to the other structures of the neck. Note how closely they are associated with the jugular vein.

tion, or novocaine (¼ or ½ percent) with adrenalin, are the most easily applied and the most satisfactory. The tissues on each side of the growth and the whole thickness of the lip well beyond the portion to be removed should be thoroughly infiltrated with the solution. The area to be excised should be outlined by a gentle scratch

with the scalpel before the infiltration is begun, as infiltration distorts the appearance of the neoplasms and renders it difficult to recognize the boundaries; hence after operation it may be found that not enough margin has been given. Before making the incision it is an advantage for hemostasis to have an assistant compress the lip on each side between thumb and forefinger. The tissue removed is generally in the shape of a wedge, with the apex down in tumor of the lower lip and apex upward in the case of the upper lip. There is a divided coronary artery to be ligated on each side, catgut be-

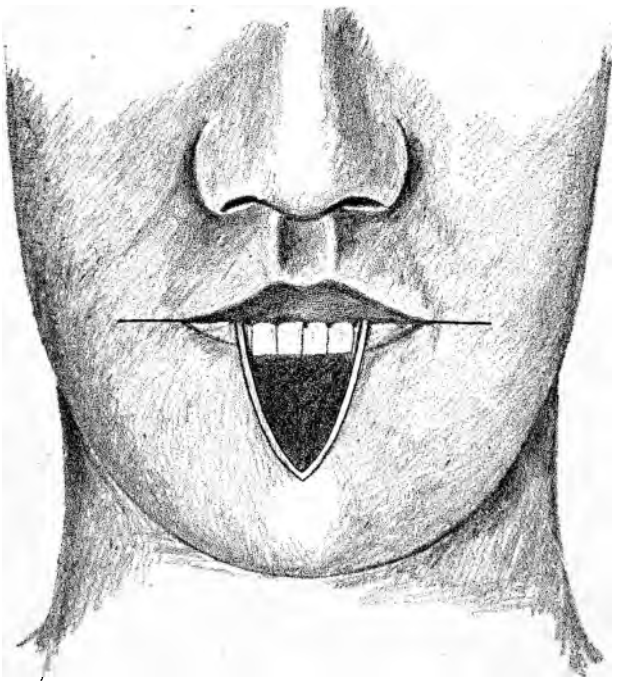

Fig. 85.—This figure and the following one show the common method of repairing a defect caused by the excision of a V-shaped piece of the lip.

ing used. Careful approximation of the skin and mucous membrane with linear continuity of the vermilion border of the lip is, of course, desirable, and is perhaps best done with fine silk or horse hair for stitches, using interrupted sutures.

Proper cleansing of the mouth and teeth before operation, giving special attention to pyorrhea alveolaris (in which case the gums should be cleansed and swabbed with tincture iodine), are important for prompt and cosmetic healing. The sutures in the skin had best be removed early, within two or three days, to prevent cross

scars. The later spreading of the wound can be prevented by adhesive strips across the wound or a collodion dressing.

Because of the frequency of the prickle-celled cancer, all sections thus removed should be examined by an expert pathologist, and, if found to be true cancer, unless of the basal-celled type or of the non-infiltrating warty variety, the operation upon the neck should be done at an early date.

Various plastic operations are used in repairing the lip after the removal of a section. The avoidance of tension and the cosmetic re-

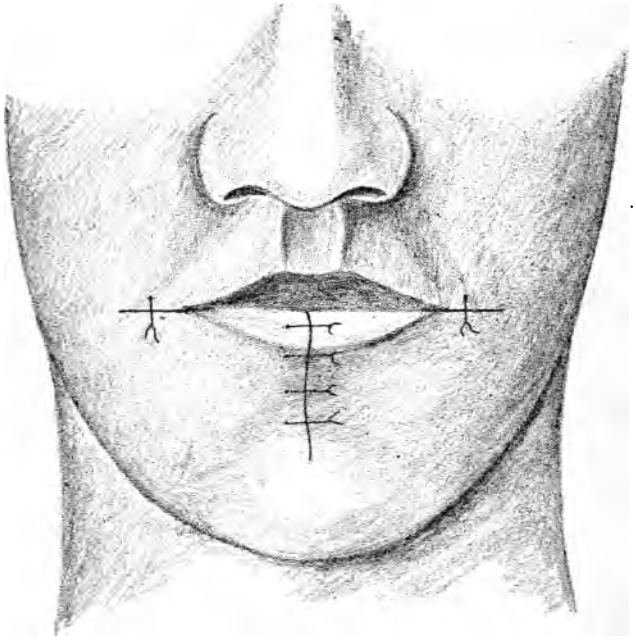

Fig. 86.—See Fig. 85.

sult should determine which of the chiloplastics is to be used in a given case. That generally used when a small lesion has been excised in the shape of a wedge is simple approximation of the edges. If the wedge removed has been a large one, and a great portion of the lip is missing, a horizontal cut can be made from the corner of the mouth upon one or both sides, carrying the incisions through the thickness of the cheek, and then the sides of the wedge drawn together without tension (Figs. 85, 86). Mayo's method of removing a quadrilateral section instead of a wedge is an improvement (Figs. 87, 88). In extensive growths, which have invaded the lip or cheek extensively, there can be no hard and fast rules for the

chiloplasty (Figs. 89, 90, 91). It is most important to give the growth a wide margin and not sacrifice complete removal to the desire for an easy closure.

As has been said above, there should preferably be no connection between the lines of incision for removal of a growth on the lip and the incision on the neck for the removal of the lymphatics. The older ingenious plastics, which combined flaps for the closure of gaps in the lip and exposure of field for removing cervical lymphatics, are obviously not to be recommended—first, because of the risk of infecting the entire field of operation from the buccal cavity, and, second, because the operation upon the cervical lymph glands cannot be complete enough.

In the hands of those expert enough in the use of local anesthetics, especially novocaine, extensive operations can be done upon the neck

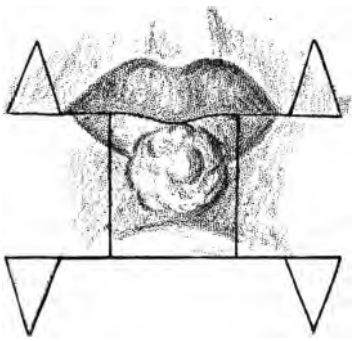

Fig. 87.—This shows the incisions used at the Mayo clinic, both for the removal of the growth and the repair of the deformity. (Redrawn after Boeckman.)

very satisfactorily without submitting the patient to the risk of a general anesthetic. The majority of surgeons, however, still prefer a general anesthetic for this part of the work. If the lip is done first, the gloves should be changed and fresh instruments and towels used for the second part of the operation upon the neck. It is generally advantageous to do the radical operation upon the neck first, and, after the neck incisions have been closed and protected, excise the portion of the lip containing the growth and repair the lip.

Extensive operations for cancer of the lip, as for cancer elsewhere—often in old men with arterial, renal, or myocardial changes—should never be undertaken without previous most careful examination of the patient's general condition and preliminary treatment according to the demands of the system.

The avoidance of shock, hemorrhage, and infection is especially necessary in these cases. A preliminary dose of morphine and atro-

pine, a carefully given anesthetic, a minimum of trauma from retraction and throat dissection, will lessen the shock. The exclusion of nervous stimuli, according to Crile's principle of anoci-association, is an important refinement in preventing shock in weak or nervous individuals. The most painstaking hemostasis is desirable, not only to avoid loss of blood, but so that structures may be more easily recognized during the operation.

The importance of making the operation upon the neck independent of that on the lip, to avoid infection, has been mentioned. When

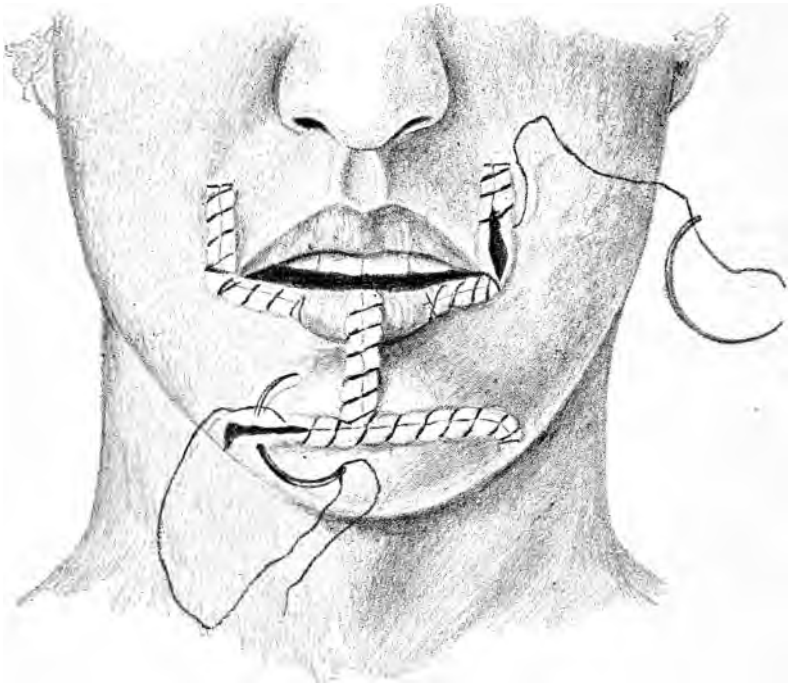

Fig. 88.—At the Mayo clinic the deformity caused by the excision of a cancer of the lip is remedied as shown above. (Redrawn after Boeckman.)

Wharton's duct is divided for removal of the submaxillary salivary gland, there is always a slight risk of infection from the mouth.

To avoid dissemination, the carcinomatous tissue should be handled carefully and not clamped or squeezed. The dissection must go beyond the tissues known to be infected; incomplete operations are worse than no operations. Inoperable cases are those in which the cancer has left the glands and invaded the deep planes of the neck. The skin may be adherent or encrusted over the submaxillary glands, and still the case be perfectly operable.

Beckman, writing from the Mayo clinic, says that their preference in cases where it is necessary to carry the dissection down to the clavicle is to do the operation in two stages. The neck is done first, and the primary growth on the lips one week later. An incision is made about three-quarters of an inch below the ramus of the jaw and extending through skin and platysma from one sternomastoid to the other. The low incision avoids the small branch of the facial artery, which innervates the muscles about the angle of the mouth. All of the fascia and fat, including the submaxillary salivary glands, are removed, and thus both submaxillary triangles and the submental triangle are emptied. The glands from the submaxil-

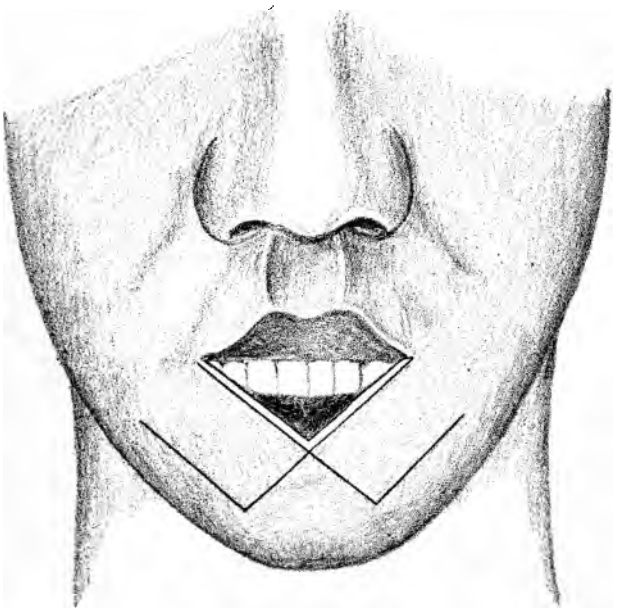

Fig. 89.—Figs. 89, 90, and 91 illustrate various plastic operations for repairing defects after removal of cancer of the lip. (Redrawn after Tilton.)

lary triangle on the side of the tumor are examined at once, and, if they are found to be carcinomatous, the incision is carried down to the clavicle on that side. All glands, including the anterior and posterior jugular groups on this side of the neck, are removed by block dissection. If the glands in the submaxillary region on the side of the neck opposite the tumor be also involved, nothing short of a block dissection of both sides of the neck is permissible. There were ninety-nine patients who had a primary radical operation done for cancer of the lower lip—that is, both the glands of the neck and

the growth excised. Cures were estimated at 83.8 percent; thirty-nine of these patients had gone three years since operation and four over five years. In eighteen cases out of the ninety-five, carcinoma was demonstrated in the glands by the microscope at the time of operation. Of these nine or 50 percent were among the cured cases. In a group where some previous operation had been done upon the lip, or it had been treated with a caustic paste, and a late radical operation was performed, the cures were 70 percent. Of this latter group showing glandular involvement, 33 1/3 percent were cured.

Crile strongly urges the neck operation as a routine in all cases

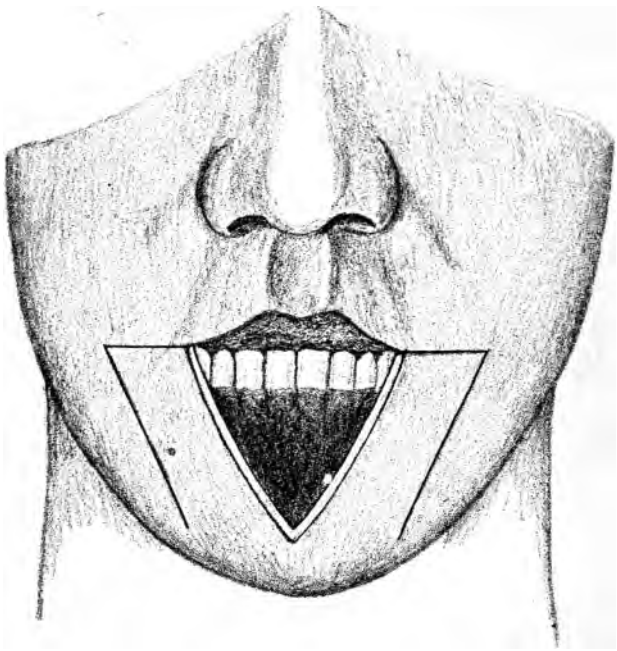

Fig. 90.—See Fig. 89.

of cancer of the lip. Where there are no palpable glands, he makes the small incision as illustrated in Fig. 92. Through this the regional lymphatic-bearing tissue is removed by block dissection. This includes both fat and glands of the submental and submaxillary region on the side of the growth. The submaxillary salivary gland is not removed if there is certainly no involvement of the regional lymphatics. In cases with definitely involved enlarged lymphatic glands the entire lymphatic-bearing tissue of that side of the neck is removed. The carotid artery is exposed as low down as possible by an intramuscular separation of the sternomastoid muscle, and

temporary closure of this artery is effected. The complete skin incision (Fig. 93) is then made (including platysma) and the flaps extensively reflected. The sternomastoid is divided, the external and internal jugular veins are secured, doubly tied, and divided at the base of the neck. The dissection is then carried from below upward (Figs. 94, 95) into the deep planes of the neck, behind the lymph glands. All the fat, fascia, muscles, veins, and connective tissue are carried upward. The dissection becomes easy when following the deep plane. The entire block of tissue is finally divided above (Fig. 96). It includes fascia, fat, submaxillary, salivary and part of the parotid glands, sternomastoid, omohyoid, part of the stylolingoid

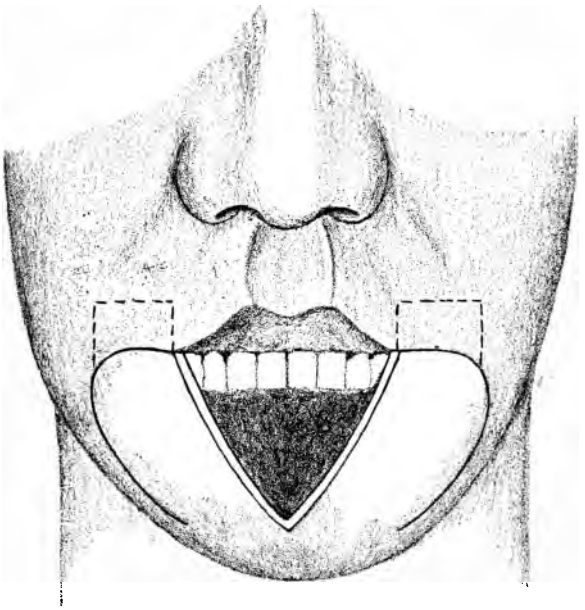

Fig. 91.—See Fig. 89.

muscles, the entire venous system, and all the lymphatic vessels and glands in this region. The key to the situation in the radical block excision of the entire side of the neck lies in the removal of the internal jugular vein. Crile has done this radical operation on both sides of the neck in the same individual in two operations, with an interval of three months between operations. Both the internal and external jugulars were removed on both sides.

Crile's radical block dissection has shown itself to be four times more effective than his former procedures.

Bloodgood urges surgeons to study their cases of cancer of the

lower lip in which the glands show metastasis. His cases showed only 50 percent of five-year cures. He does not think that the operation on glands has been complete enough, and believes that a portion of the parotid and the submaxillary salivary glands should be included in the block. The subparotid lymph glands have been left behind in recent operations, for he feels that it is impossible to completely remove these glands without the ligation and excision of the upper portion of the internal jugular behind which they lie. The

Fig. 92.—When the glands are not palpably involved, this incision should be made. (Redrawn after Crile.)

operation for recurrent cancer of the lip reduces the probability of a cure at least 42 percent.

In cases of cancer of the upper lip the simple local operation can be more often done, because the majority of cancers here are of the basal-celled variety. When a prickle-celled tumor is, however, situated on the upper lip, the same operation is indicated as for cancer of the lower lip.

Conclusions.—In conclusion, it must be said that cancer of the lip is a serious and frequent malady, and that it may develop within two months after the onset of an apparently simple malady. Benign and precancerous lesions occurring here should be excised early

and histologically examined to make sure of their character. None of the lesions should be treated the way skin lesions may be treated —that is, by caustics, cautery, carbon-dioxide snow, x-ray, radium, etc. The rarer basal-celled tumors and the malignant warts do not require more than a careful local excision.

All squamous-celled cancers should have not only local removal, but also removal of the glands of the neck.

The local operation can readily be done with local anesthesia, and

Fig. 93.—When the glands are clearly involved, this incision should be made. (Redrawn after Crile.)

under proper conditions the radical operation can be performed in the same way.

The slight tendency for the growth to go beyond the cervical lymph glands and the accessibility of these glands should encourage more radical and painstaking operations.

Where the submaxillary glands are known to be definitely involved, the entire lymphatic chain on that side of the neck should be removed by block dissection, including the internal jugular vein.

Tongue.—Like all other cancers of the skin and mucous membranes, carcinomata of the tongue do not arise *de novo*, but from some pre-existing lesion. There is first an ulcer or a little area of infiltration

that should give plenty of warning. These precancerous lesions may arise in various ways; they may be due to the irritation caused by bad teeth, or they may result from the excessive use of tobacco, either smoked or chewed. The latter must play some part, for cancer of this organ is very rare in women. Small papillary outgrowths of

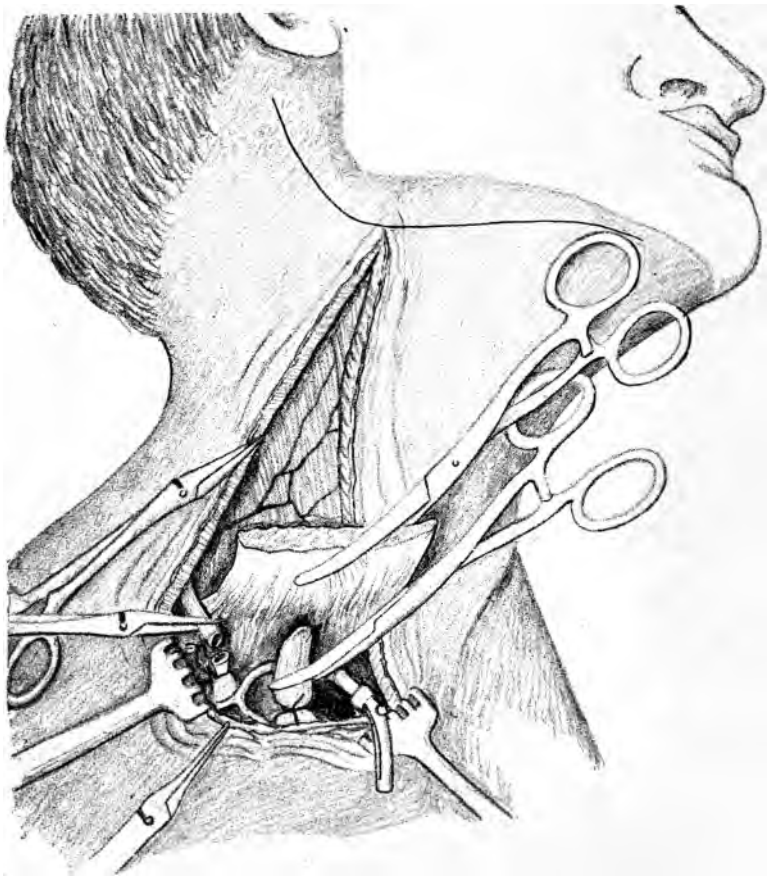

Fig. 94.—After the skin and subcutaneous tissue have been incised, the sternocleidomastoid muscle is divided, the jugular veins ligated and cut, and the carotid artery is clamped. The skin and platysma are then dissected back. (Redrawn after Crile.)

the tip or the lateral edges of the tongue are rather infrequent, but nevertheless do occur, and, even where there is no deep infiltration, they should always be removed, preferably with the electric cautery.

Syphilis is probably the most frequent cause of cancer of the tongue. Syphilis may produce either ulcers or superficial over-

growths, and these are very apt to undergo malignant change, especially in heavy smokers. The well-known leukoplakia, the so-called psoriasis or smoker's patch of the tongue, is often due to syphilis, although the use of tobacco must play a very important part. This

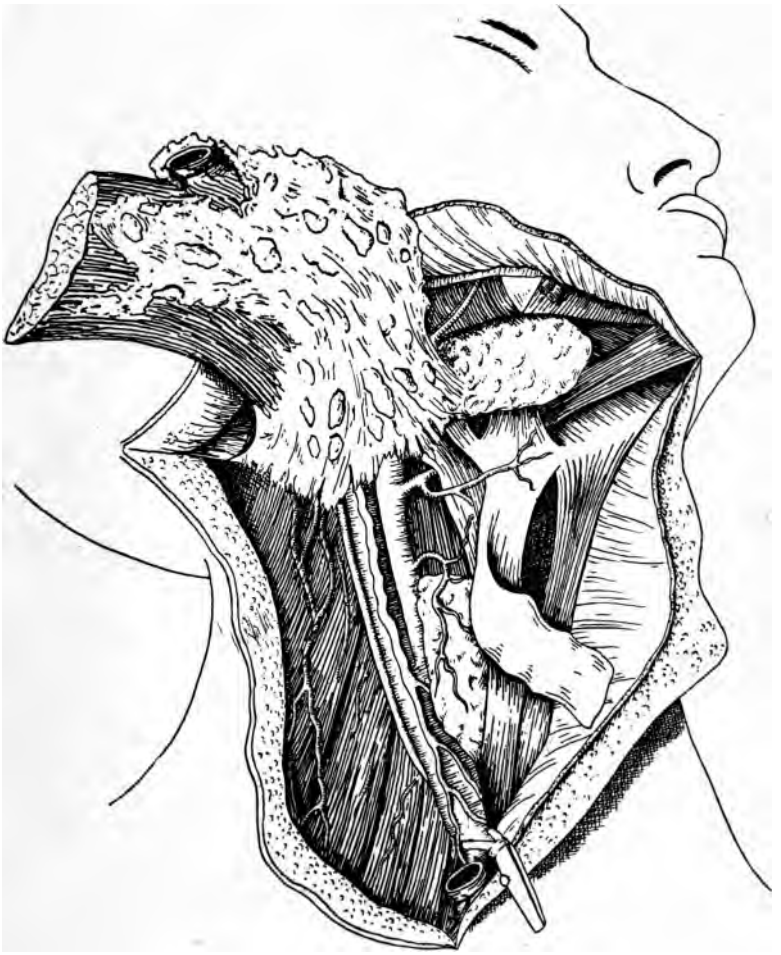

Fig. 95.—The entire mass of lymph gland-bearing tissue is then excised en bloc. The dissection must be done in the deep plane of the neck. (Redrawn after Crile.)

ailment is characterized by the presence of superficial, white, slightly indurated patches, that have a tendency to form deep cracks and fissures. Many of them subsequently degenerate into true cancer. When leukoplakia is first seen, a thorough search for syphilis should

always be instituted, and, if that is present, antisyphilitic medication should be pushed; in addition, smoking must be absolutely prohibited. If syphilis be not present, smoking should be forbidden and mild mouth wash prescribed. If the lesions yield promptly, as they

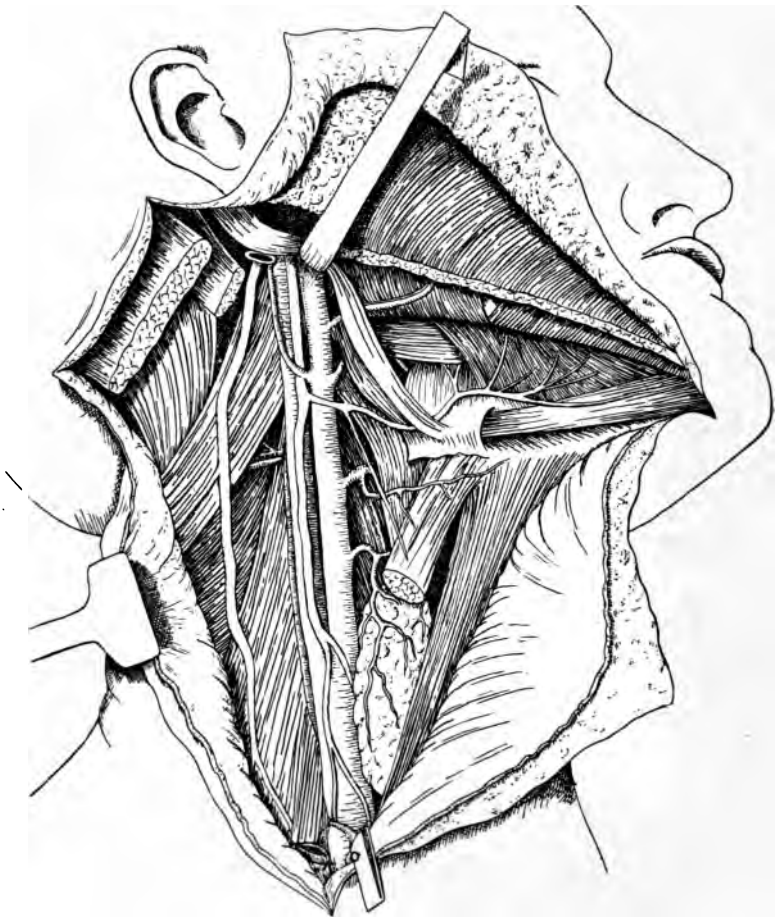

Fig. 96.—All gland-bearing tissue has been removed, and the wound is ready to be closed. (Redrawn after Crile.)

sometimes do, operative treatment is not necessary, but, if the lesions still persist and especially if they increase in size, they should be thoroughly removed, preferably by either the actual or the electric cautery. In no case should they be touched with mild caustics or with any irritating substances; this is the worst thing that could

possibly be done, for any form of irritation, short of complete removal, may stimulate cancerous changes.

Tuberculous ulcers may likewise become cancerous, but, as a general rule, tuberculous lesions are rare, except in advanced tuberculosis of the lungs or in a generalized tuberculosis.

Any crack, fissure, or nodule should be viewed with suspicion until it is proven not to be cancerous. There are, of course, a number of lesions of the tongue that are perfectly benign; such a one is lichen planus, which often involves the mucous membranes of the cheek and which may invade the tongue. Occasionally we find a superficial infiltration of the surface, an infiltration that is sharply localized and rather angular, and that is most apt to occur in those who use either tobacco or snuff, and which seems to remain harmless. But in all cases of any abnormality a skilled man should be consulted.

Varieties.—Various types of cancer may occur upon the tongue, but the common one is the spino-celled carcinoma, the type that speedily metastasizes. Cubo-celled growths also occur, but they are of mere pathological interest, for they are nearly as deadly as is the type just mentioned. The spino-celled wart also rarely occurs here; fortunately it does not metastasize, so local removal will suffice to give a cure. Basal-celled cancer, and rodent ulcers are extremely rare, and such a diagnosis should be received with the greatest caution. The pathology of all of these growths is identical with that of those already described.

Symptomatology.—Cancer may develop upon any part of the tongue, but usually upon the dorsum near the edge, this being the part most exposed to trauma. Occasionally they develop primarily upon the floor of the mouth. As already indicated, there is always a precancerous lesion; it is noted that either deep induration or ulceration, or both, has taken place around this, and that an indurated ulcer, rarely a fungous tumor, results. Glandular involvement may occur within one month, and is rarely postponed more than six months. The floor of the mouth is often infiltrated at a very early date, nearly always within six months.

Diagnosis.—The first difficulty is to determine whether a precancerous lesion has actually taken on a cancerous change, and how long this change has existed; this is always extremely difficult, for it is much easier to diagnose a late cancer than it is an early cancer, the only trouble being that, when a carcinoma is easily diagnosed, it is not easily cured. Hence there is only one safe rule, and that is

to treat all such lesions as early cancers, and to have live patients at the end of a few years. In certain instances it is almost impossible to distinguish a gummatous lesion from a cancer. When one remembers that cancer so frequently develops upon a syphilitic basis, it can be readily seen that the Wassermann reaction is more apt to prove a hindrance rather than an aid. In case of doubt, and if the lesion is advanced, it is well to give two or more intravenous in-

Fig. 97.—This cancer of the tongue is of four months' duration. It had been treated with various caustics, which had apparently hastened its growth. (Photograph by Dr. Walter Van Swerirgen of Dr. H. H. Kerr's patient.)

jections of salvarsan at close intervals and watch the result. In the case of a small lesion the same procedure may be tried, or the whole lesion may be excised with the cautery and then studied microscopically. Tuberculous lesions may also be difficult to distinguish. In the case of very advanced tuberculosis it makes very little difference what the lesion is, but in other cases the differential diagnosis may be a matter of extreme importance. The whole lesion should be excised with the cautery, and the central portion studied microscopical-

ly and a bit of the fresh tissue injected into a guinea pig. This last is important, because tuberculosis may histologically resemble carcinoma.

Treatment.—Bloodgood[25] has recently written a short, but stimulating, article on treatment of cancer of the tongue. He states that in the very early cases—that is, where malignant change is just taking place— a complete local removal with the cautery will nearly always effect a cure. Referring to the later cases, Bloodgood states:

"It has been demonstrated that the failure to cure when the cancer of the tongue is fully developed is due to the neglect to remove the muscles of the floor of the mouth below the cancer.

"The high mortality after operations for cancer of the tongue is chiefly due to the removal of the floor of the mouth without removing at the same time a section of the lower jaw.

"When the operation is performed in one stage, it is impossible to remove the tongue, the floor of the mouth, the glands, and then close the opening in the mouth unless a section of the lower jaw is also removed. If the former operation is done thoroughly, the mortality is very high—almost 80 percent—from primary or secondary pneumonia, or late infection from the oral fistula."

For moderately early cases Bloodgood recommends an operation done along the following lines: The glands of the neck are first thoroughly removed, and the floor of the mouth above the glands, but below the tongue, thoroughly burned with the cautery, and the wound closed. At a little later date the affected portion of the tongue and the floor of the mouth below it are attacked from above with the cautery until the two areas of cauterization meet. The healed skin flap from the first operation forms the floor of the mouth and prevents infection from without.

In very late cases it is still necessary to remove a section of jaw, the tongue, floor of the mouth, and glands in a block operation.

Trunk.—Cancer of the trunk is rather uncommon, although the most frequent site is around the shoulders. In this locality the majority of growths are of basal-celled origin, and do not metastasize. Upon other portions of the body prickle-celled growths predominate, and they should always be removed, together with the draining glands, by a block operation, as otherwise recurrence is very apt to follow.

About the breast we may find Paget's disease of the nipple or a

[25] Bloodgood: South. Med. Jour. 1914, vii, 542.

carcinoma *en cuirasse*. The latter is very rare, but must be thought of when nodules appear upon the skin in the vicinity of the mammary gland.

Extremities.—The following account is from a recent article by the author.[26]

Because of the failure to distinguish between the various types of cutaneous cancer, many of the older articles on carcinoma of the extremities are practically worthless from a modern point of view. Howard Fox[27] has recently reported an interesting case of cancer of the hand which metastasized to the mediastinal glands, and has reviewed the literature. After studying various articles, notably those by Heimann,[28] Gurlt,[29] von Winiwarter,[30] Neumann,[31] Bulkley and Janeway,[32] von Brunn,[33] Volkmann,[34] and Franz[35] he comes to the conclusion that cancer of the limbs is comparatively a rare disease as compared with cutaneous cancer in other portions of the body. Fox, referring to cancer of the hand, further says: "In spite of the malignancy of these cases from a microscopical standpoint, there can be no doubt that clinically they are relatively benign, generally running a slow course, and only late, if at all, invading the lymphatic glands." On the other hand, in a discussion[36] of this paper, both Schalek and Corlett reported cases in which metastases had occurred, while Wile called attention to the fact that cancers originating in arsenical keratoses usually metastasized.

Bloodgood[37] has consistently contended that the lymphatic glands should be removed in all cases of prickle-celled cancer of the body, no matter where located, but especially on the limbs, for here is it always easy to remove the draining lymphatics. Steiner,[38] writing from the clinic of Dollinger, states that a routine practice is made of removing lymph glands in all cases of cancer of the extremities. A summary of the literature would seem to indicate that cutaneous cancers of the extremities are not especially common, that they are

[26] Hazen: Jour. Amer. Med. Assn., 1915, lxv, 837.
[27] Fox: Jour. Cutan. Dis., 1915, xxxii, 22.
[28] Heimann: Arch. f. klin. Chir., 1898, lvii, 911.
[29] Gurlt: Arch. f. klin. Chir., 1880, xxv, 421.
[30] von Winiwarter: Beiträge zur Statistik der Carcinome, Stuttgart, 1878.
[31] Neumann: Beitrag zur Kenntnis der Extremitäten-Krebse im Anschluss an zwei Fälle der Freiburger Klinik, Inaug. Diss. Freiburg im Breisgau, 1911.
[32] Bulkley and Janeway: Med. Record, New York, lxiii, 465.
[33] Von Brunn: Beitr. z. klin. Chir., 1903, xxxvii, 227.
[34] Volkmann: Samml. klin. Vortr., 1889, No. 102.
[35] Franz: Beitr. z. klin. Chir., 1902, xxxv, 171.
[36] Discussion: Jour. Cutan. Dis., 1915, xxxiii, 29.
[37] Bloodgood: Progressive Medicine, Dec., 1904, 1907, 1908, 1912.
[38] Steiner: Deutsch. Ztschr. f. Chir., 1906, lxxxii, 363.

more common on the lower than on the upper limbs, that they always follow some precancerous conditions, that they are usually of the prickle-celled type, that they are rare on the palms of the hands, and that when occurring on the backs of the hands they are relatively benign. Regarding their tendency to form metastases, there is considerable diversity of opinion.

With a view of clearing up the last point, which is of great practical importance, especially now that radium, the Röntgen rays, fulguration, desiccation, and similar nonoperative procedures are making great bids for the treatment of these conditions, the author presents the statistics shown in table 2, derived largely from Dr. Bloodgood's surgical-pathologic laboratory of the Johns Hopkins Hospital, from the surgical wards of the Freedmen's Hospital, and from the writer's practice.

TABLE 1.—DISTRIBUTION ON UPPER AND LOWER LIMBS OF THE VARIOUS TYPES OF CANCER.

	Prickle	Malignant wart	Cuboidal	Basal	Malignant mole
Upper limb	19	5	0	4	1
Lower limb	18	0	4	6	1
Total	37	5	4	10	2

There was a total of fifty-eight cases. It will be readily seen that the commonest tumor is the spino-celled one, and that the basal-celled one ranks next. Malignant warts are much commoner on the upper than on the lower extremity, while the reverse is true of the cuboidal-celled carcinomas. Cancer of the upper limb is just about as common as is cancer of the lower limb.

Prickle-celled growths originated in precancerous dermatoses, and metastasized as shown in table 2.

TABLE 2.—METASTASES OCCURRING IN PRICKLE-CELLED GROWTHS.

Origin	Total cases	Cases followed three years	Metastatic cases
Röntgen ray dermatitis	2	2	2
Scar of burn	8	5	3
Scar of trauma	6	4	1
Ulcer	2	0	?
Wart	7	2	2
Senile keratosis	2	1	0
"Pimple"	4	3	1
Arsenic keratosis	1	1	1
Blastomycosis	1	1	0
Bone sinus	1	0	?
Undetermined	3	1	1
Total	37	20	11

The observation that cancer originating from Röntgen ray dermatitis and from arsenic keratosis usually metastasizes is borne out here. Cancer springing from the scars of burns has given a rather high percentage of metastatic growths.

With respect to the influence that location of the primary growth has on the liability to metastatic formation, table 3 is presented.

TABLE 3.—METASTASES WITH REFERENCE TO LOCATION OF PRIMARY GROWTH.

	Total cases	Cases followed three years	Metastatic cases
Finger	4	2	2
Back of hand	8	3	1
Wrist	1	0	?
Forearm	1	0	?
Elbow	2	1	1
Upper arm	3	2	1
Foot	2	2	1
Ankle	3	1	0
Lower leg	7	4	2
Knee	2	2	1
Thigh	4	3	2

In such a small series of cases it is impossible to determine just what influence position has on the liability toward metastasis, but it would appear to have very little. The high percentage of metastases in the followed cases is notable. It will probably be objected that most of these cases were surgical ones, and that they were severe cases and of long duration. Now, as a matter of fact, in six of the metastatic cases the primary cancerous changes had been present for three months or less. In one notable case there was a cancer of the lower leg that had existed for two months. Under divided doses of the Röntgen rays the primary growth healed and stayed healed, but five years later metastases developed in the inguinal glands and the patient succumbed. In the other ten instances recurrence in the glands followed amputation in five cases and local surgical removal in five. The nine patients who stayed cured for more than three years were all subjected to local operation alone.

A study of these few figures should clearly show that prickle-celled cancer of the skin is comparable to cancer of the breast, tongue or lips, and, just as no good surgeon would think of treating a true cancer of these organs by local removal alone, so should he shrink from the mere local removal of an analogous condition of the cutis. In many instances it is impossible to determine the exact nature of

a cutaneous cancer. Here the correct procedure is undoubtedly to excise the entire growth and then make a study of it. To attempt to cure a malignant neoplasm of the limbs without first ascertaining its nature is both foolhardy and dangerous, to say the least, and will undoubtedly result in the sacrifice of many lives.

There were four cases of cuboidal-celled cancer, one of which originated from a varicose ulcer of the leg and was cured by the cautery. One developed on the scar of a bed sore on the thigh and was cured by local excision. Another originated in a senile keratosis on the thigh and recurred in the inguinal glands seventeen months after local excision. The last occurred in the scar of a trauma on the thigh, and promptly recurred in the inguinal glands after local excision. All growths were of less than one year's duration. All were in women. It is plainly evident that cuboidal-celled cancer is analogous to spino-celled cancer in the way that it metastasizes, and that it should be treated accordingly.

There were five cases of malignant warts—three on the back of the hand, one on the wrist, and one on the forearm. All originated in warty growths. Bloodgood (see page 212), in a careful study of malignant warts, comes to the conclusion that they never metastasize and that complete local removal is sufficient to effect a cure. Yet in one case in this series metastasis and death did follow a local operation, probably not a complete one. Inasmuch as these growths are more common on the back of the hand than elsewhere, inasmuch as they show a spino-celled structure, and inasmuch as they very rarely metastasize, it is probable that those who have stated that cancer of the hand is a benign affection have had most of their experience with this variety of tumor.

There were ten basal-celled cancers, which arose from the following dermatoses:

Ulcer	6
Scar or burn	1
Pigmented mole	1
"Pimple"	1
Nodule	1

They arose in the following areas:

Finger	1
Hand	1
Upper arm	2
Ankle	1
Lower leg	4
Thigh	1

In one remarkable case the glands later developed metastatic growths that showed all of the peculiarities of a spino-celled carcinoma. So far as known, there were no other metastases in this group.

In two instances there were multiple melanotic growths, secondary to pigmented moles. One occurred on the arm of a woman who had suffered but a single trauma to a pigmented mole. This immediately ulcerated and was excised, but promptly recurred. During the next five years there were a number of local operations. She then entered the hospital with a mass of inoperable glands in the axilla, but with no signs of metastatic growths in the body. It is more than probable that a complete early operation, including the axillary glands, would have resulted in permanent cure. The other instance occurred in a negro man, this being probably the only case on record of a malignant mole in one of his race. The primary growth was in the sole of the foot. There were metastases both to the glands and to the lungs, and death speedily ensued.

Penis.[39]—Cancer of the penis is not especially common, although certain authors state that it constitutes nearly 1 percent of all cancers, undoubtedly entirely too high an estimate.

None of the text-books or articles that the author has read has given a correct account of the pathology of these cancers, which are analogous to those occurring upon the lip. In other words, there are three varieties—first, the common prickle-celled variety; second, the prickle-celled malignant warts; and third, the basal-celled growths. Cuboidal-celled tumors also occur very exceptionally, thus really making four varieties.

The common malignant tumors are the squamous-celled ones, that usually originate on the glans penis or mucous membrane of the foreskin, and that speedily ulcerate and fungate. Metastases to the inguinal glands are nearly always present after a short time, and hence in dealing with these growths it is necessary not only to remove the local growth, but also to do a complete dissection of the glands on both sides. This should be done as upon the lip, making a block dissection, first removing the glands and then amputating the penis. Where this is not done, there are practically no recoveries, but, where this operation is performed in early cases, the percentage of cure is above 36 percent.

The prickle-celled malignant warts may be mistaken for venereal warts, but speedily ulcerate. There is, however, no induration about the base, and an extensive local removal will result in a permanent

[39] Barney: Annals of Surg., 1907, xlvi, 890, 244.

cure. In many of these cases it is necessary to amputate the end of the penis, but this is not always necessary.

The basal-celled tumors resemble other members of this group, sometimes acting as do the slowly growing rodent ulcers, and sometimes forming fungating masses, which have a much smoother surface than the squamous-celled neoplasms. Local removal will suffice to effect a cure.

The cuboidal-celled growths, as already stated, are formed from the transitional epithelium normally lying between the basal and prickle layers. They form either fungous tumors or ulcers. Treatment is the same as for the squamous-celled growths.

It is generally conceded that many cancers of the penis arise from phimosis and retained secretions, and that perfect cleanliness would markedly limit their number.

Vulva.—Tumors of the vulva are practically identical with those upon the penis, the largest number being of the very malignant type. Treatment requires not only local excision, but removal of the inguinal glands as well.

Anus.—Considering the trauma (due to the passage of feces) to which the anus is continually subjected, it is surprising how rare tumors of this region are. The majority of the malignant tumors arise from the squamous epithelium of the rectum near the anal margin, and run a course typical of the prickle-celled tumors in general. Metastasis may take place to the inguinal glands or to the lymphatic glands in the pelvis.

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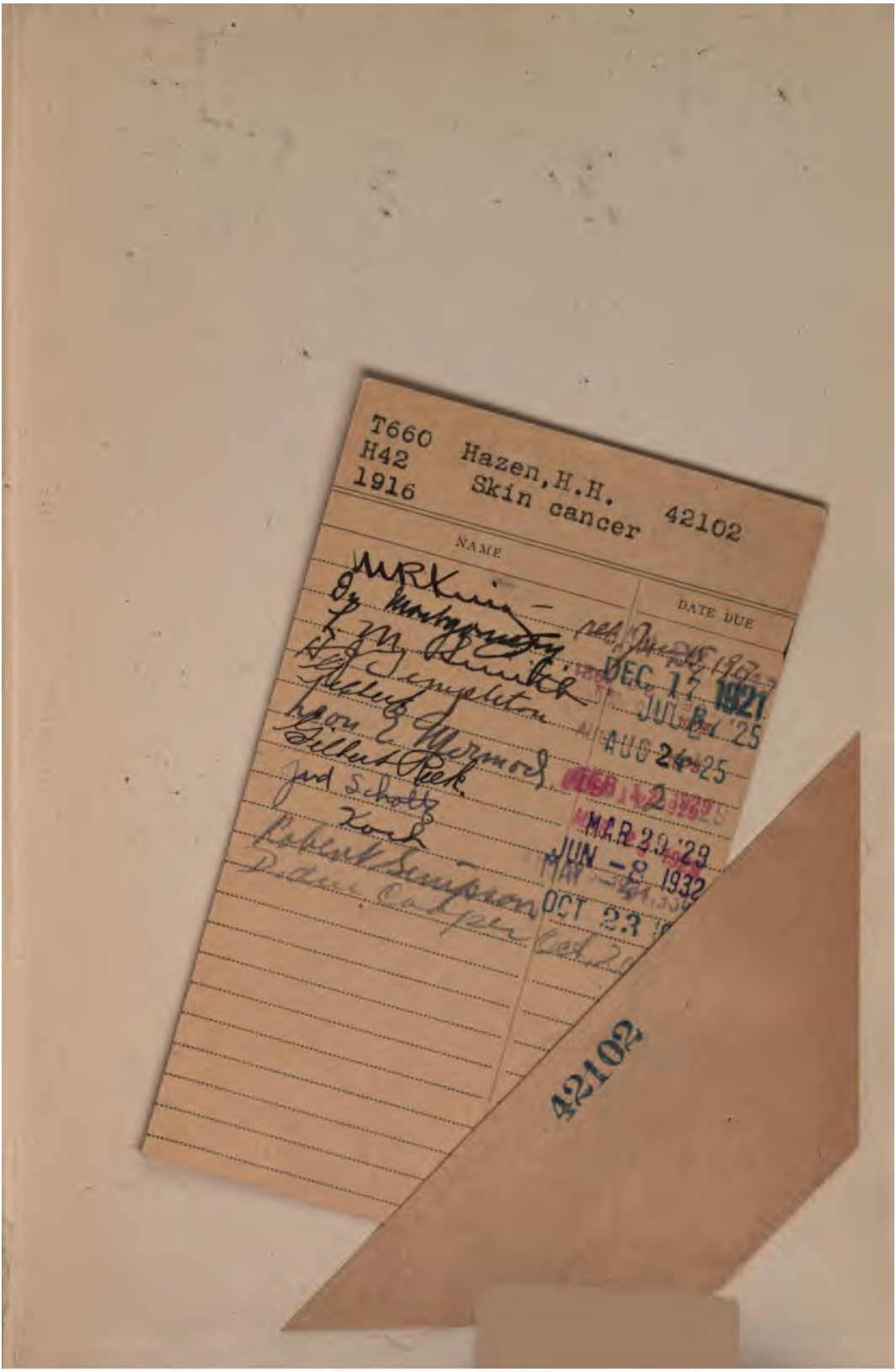
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